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THE DIAGNOSIS OF HYPOTHYROIDISM IN CHILDHOOD

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When severe thyroid deficiency has existed over a considerable span of time during the early years of growth, it gives rise to the classic clinical pictures described as cretinism or as juvenile hypothyroidism, which are readily recognized. Many cretins, however, when seen in the first year or two of life, are less grotesquely abnormal, and on superficial inspection might be mistaken for fairly normal infants considerably younger than their actual age. In studying dwarfs of an older age, one finds almost innumerable variations and gradations from the broad, stocky build of the typical person with hypothyroidism to the slender, wiry, small-featured dwarf who presents no suggestion of thyroid deficiency.

Great differences of opinion have arisen as to what constitutes the signs of hypothyroidism in cases not presenting the frank, typical picture. In recent years there have been a lack of critical analysis and an excess of enthusiasm, so that the diagnosis of hypothyroidism has been made often on the finding of some one suggestive sign. If a child's eyes are widely spaced or his nose is flat or if he is mentally retarded or physically stunted, he may be diagnosed a cretin. In fact, almost any infant who is retarded in development or who is peculiar or ugly runs the chance of being branded as having hypothyroidism. Since most physicians are aware that epiphysial ossification is delayed in hypothyroidism, roentgenograms of the bones are usually made. If retardation of osseous development is found, the physician considers that the diagnosis of hypothyroidism is proved. Dryness and coarseness of the skin and hair or a dull, phlegmatic disposition likewise may lead to uncritical diagnoses. The numerous variations in type among dwarfs give the endocrinologist opportunities for wide flights of fancy which alight on such diagnoses as thyropituitary, pituitarothyroid and thyrohypogonadal deficiencies, although there is often no real proof of either thyroid or pituitary deficiency.

The existence of "borderline" forms of hypothyroidism or of mixed endocrine disturbances should not be denied, nor should the therapeutic trial of thyroid be discouraged in doubtful cases. However, the limitations of our present knowledge should be frankly recognized and the need for diagnostic humility emphasized. It seems worth while, therefore, to review and to attempt to evaluate the physical signs resulting from thyroid deficiency in childhood and to discuss some of the recent studies of the functional or biochemical changes.

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CLASSIFICATION OF PHYSICAL SIGNS

In adults, many of the familiar physical signs of hypothyroidism depend on a lowered rate of metabolism and alterations in the circulation. In addition, abnormalities in chemical processes of the body are responsible for some of the characteristic changes in subcutaneous tissues, skin, hair and muscle to which the term myxedema has been applied. In childhood, thyroid deficiency gives rise to additional changes due to its influence on growth and development.

In table 1 are listed the most important signs which result from hypothyroidism during the period of growth. These signs have been divided into anatomic alterations in bodily structure and functional or physiologic alterations. The structural changes which are the most characteristic and the most constant are those caused by defective growth and development of the skeleton. These are stunted growth, infantile skeletal proportions, infantile naso-orbital configuration, retarded skeletal development, delayed and defective development of the teeth and epiphysial dysgenesis. The changes in other structures of the body are less characteristic and are encountered much less constantly. Frequently the hair is entirely normal and there is little, if any, change in the skin. Thickening of subcutaneous tissues and soft parts such as the lips and tongue may be suggestive of the diagnosis when found; but such changes may not be advanced, and true myxedema is rarely as extreme as in the adult.

SKELETAL CHANGES

The skeletal changes must be considered in some detail.

Stunted Growth.—The rate of growth is invariably slowed in hypothyroidism. In a young cretin, who may be only 1 or 2 inches (2.5 or 5 cm.) below the average height, the dwarfing may not impress the observer. However, if a cretin remains untreated he lags more and more below the normal standards until stunting becomes apparent. During the juvenile period extreme degrees of hypothyroid dwarfism are encountered. On the other hand, if thyroid deficiency does not occur until later childhood—for example the tenth or twelfth year—the patient will have attained such a height before the cessation of growth that he cannot be classified as a dwarf.

Hypothyroidism is one of the most important causes of dwarfism. In the past five years we have studied 64 dwarfs in whom disease of bone and cardiac, renal, intestinal, hepatic and metabolic disorders could be excluded as etiologic factors. Among these, 16 patients (25 per cent) definitely had hypothyroidism. In the remainder, the cause of dwarfism could not be deter-

mined. They were presumed to have either pituitary insufficiency or "primordial dwarfism." In all but 1 of the 16 patients with hypothyroidism therapy with thyroid caused a rapid acceleration of growth, whereas similar doses of thyroid had little if any effect on the other types of dwarfism, as shown in figure 1. In the 1 patient who presented characteristic clinical and biochemical evidences of hypothyroidism but who showed no acceleration of growth on treatment with thyroid there was probably some other endocrine deficiency in addition to hypothyroidism. This case is discussed further at the end of the paper.

Skeletal Proportions.—The ratio of the upper and lower skeletal segments is determined as follows: The standing height is measured. The lower segment is measured from the top of the symphysis pubis to the floor. The length of the upper segment is found by subtracting the lower segment from the total height. According to the tables of Engelbach [1] the ratio of the upper to the lower segment is about 1.7 to 1.0 at birth. The lower segment, however, normally grows more rapidly than the upper, so that at the age of 5 years the ratio is 1.2 to 1.0 and at 10 or 11 years 1 to 1. The various opinions expressed by different authors concerning the skeletal proportions of children with hypothyroidism have been discussed by de Quervain and Wegelin.[2] It has been our experience that as the child with hypothyroidism grows older not only is growth retarded but the ratio of the skeletal segments remains that of a younger child, corresponding to the height age instead of the chronologic age.[3] On the other hand, most dwarfs who do not have hypothyroidism attain the skeletal proportions approximately normal for their actual age, although this is not invariably true. This is illustrated in figure 2.

Naso-Orbital Configuration.—The characteristic facies so frequently seen in the child with hypothyroidism is due largely to the peculiar naso-orbital configuration. The bridge of the nose is flat and broad, causing the eyes to appear widely spaced, and the nose is short and undeveloped. De Quervain and Wegelin [2] have attributed the abnormality to failure of growth at the spheno-occipital synchondrosis and disproportions in the development of the sphenoid bone. Dye and Maughan [4] have shown in experimental animals that the growth of endochondral bone is retarded while that of membranous bone is not. It seems to us that the hypothyroid facies is caused, at least partly, by the persistence of infantile characteristics, just as the proportions between the upper and lower skeletal segments remain infantile. The normal development of the features, and especially of the nose, is delayed, so that the child of 5 or 6 years with hypothyroidism often shows the naso-orbital conformation of an infant 1 or 2 years old.

TABLE 1.—*Classification of Signs*

Structural changes	
Skeleton	
	Height—stunted
	Skeletal proportions, upper : lower segment—infantile
	Naso-orbital development—infantile
	Osseous development—retarded
	Dental development—retarded and defective
	Epiphysial dysgenesis—frequently present
Other structures	
	Brain development—retarded
	(Skin—variable)
	(Hair—variable)
	(Subcutaneous tissues—variable)
Functional changes	
	Physical and mental torpor
	Peripheral circulation poor—skin pale, grayish, cool
	Pulse rate × pulse pressure—decreased
	(Sweating—variable)
	Constipation
	Biochemical and metabolic changes

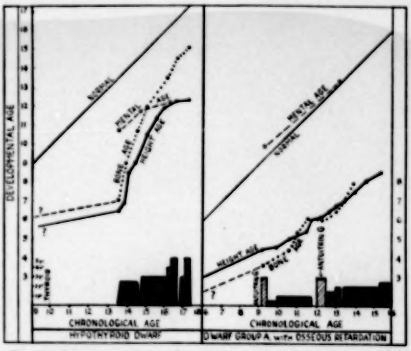

Fig. 1.—Comparison of the effect of thyroid treatment on a dwarf with hypothyroidism and on a dwarf showing a similar degree of osseous retardation but presenting no evidences of thyroid deficiency. Treatment caused a rapid acceleration of the rates of growth and osseous development in the hypothyroid patient but had little effect on the other dwarf.

Retardation of Osseous Development.—It has been known for many years that hypothyroidism always causes delay in the appearance of ossification in the cartilaginous centers. Treatment with thyroid causes an immediate acceleration in the rate of osseous development. We [5] have found that by following the rate of osseous development during treatment one can determine whether an adequate dose of thyroid is being given.

In recent years, some clinicians unfortunately have jumped to the conclusions that the thyroid gland alone controls the ossification of the cartilages and that retardation of osseous development is pathognomonic of hypothyroidism. Diagnoses of so-called borderline hypothyroidism or of mixed thyropituitary dwarfism have been based on this sign alone. We are convinced that this practice is fallacious. Endochondral ossification is at times definitely delayed in conditions which are not hypothyroid in origin. Among 50 dwarfs, in whom no evidences of thyroid deficiency were detected by means of any of the studies which we shall describe, 30 (60 per cent) showed delay of two to six years in appearance of the centers of ossification. In many instances the degree of retardation was as great as in patients with hypothyroidism. In these cases thyroid medication caused slight, if any, acceleration in the rate of osseous development, in contrast to the specific, rapid acceleration which occurs in patients with hypothyroidism. This is illustrated in figure 1.

1. Engelbach, William: Endocrine Medicine, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

2. de Quervain, Fritz, and Wegelin, C.: Der endemische Kretinismus, in Aschoff, Ludwig; Elias, Herbert; Eppinger, Hans; Sternberg, Carl, and Wenckebach, K. F.: Pathologie und Klinik in Einzeldarstellungen, Berlin, Julius Springer, 1936, vol. 7.

3. Although the shortening of the lower extremities in hypothyroidism is largely attributable to the persistence of an infantile characteristic, shortening and deformity of the necks of the femurs may also contribute to it.

4. Dye, J. A., and Maughan, G. H.: The Thyroid Gland as a Growth-Promoting and Form-Determining Factor in the Development of the Animal Body, Am. J. Anat. **44**: 331 (Nov.) 1929.

5. Wilkins, Lawson: The Rates of Growth, Osseous Development and Mental Development in Cretins as a Guide to Thyroid Treatment, J. Pediat. **12**: 429 (April) 1938; Thyroid Medication During Childhood, J. A. M. A. **114**: 2382 (June 15) 1940.

Defective Dental Development.—This subject cannot be discussed in detail in this paper. The development of the teeth is always retarded, and the delay is usually proportional to that in the endochondral ossification. In addition, the teeth which erupt during the period of thyroid deficiency are defective in structure and undergo early caries.

Epiphysial Dysgenesis.—This is probably the most specific of all the anatomic changes which are found in hypothyroidism. It is due to a disorder of the cartilages of the epiphyses and round bones leading to irregularities in their subsequent ossification. Normally, ossification begins from a single small focus in the center of the cartilage and extends peripherally in an orderly manner. If thyroid deficiency exists during the period in which ossification normally occurs, the appearance of the deposition of calcium is considerably delayed, as we have already pointed out. When calcification finally occurs, it appears as multiple, small, irregular foci scattered over a considerable area of the cartilage. These grow larger and coalesce to form a single irregular center. According to the stage of the process, the roentgenogram may show multiple small centers of ossification or a single center which may appear either stippled, porous, fluffy or fragmented. Various stages in the ossification of the head of the femur in children with hypothyroidism are shown in figure 3. In the head of the femur the condition often cannot be differentiated in the roentgenogram from Perthes' disease. The two conditions, however, are entirely unlike in their pathogenesis. Perthes' disease is a destructive process involving an epiphysis which has previously been normally formed; in hypothyroidism there is an abnormality in the development of the cartilage and its conversion into bone. Although hypothyroid epiphysial dysgenesis is observed most frequently and is most spectacular in the heads of the femurs and the navicular of the tarsus, it involves all the endochondral centers in which ossification normally

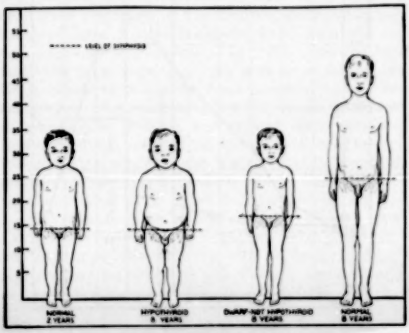

Fig. 2.—Diagram showing that the skeletal proportions of dwarfs with hypothyroidism correspond to the "height age," while those of other dwarfs correspond to the chronologic age.

occurs during the period in which the deficiency exists. It can be found if roentgenograms are taken frequently enough to show the earliest appearance of calcification. From the paucity of American literature on the subject one might suspect that the condition is relatively rare in sporadic cretinism, although it has been encountered by some workers in a large proportion of patients with endemic cretinism. However, in reviewing serial roentgenograms of the bones of 25 children with hypothyroidism one of us [6] found epiphysial dysgenesis in all but 2 cases. In these 2 cases roentgenograms had been taken only at long intervals after treatment was begun.

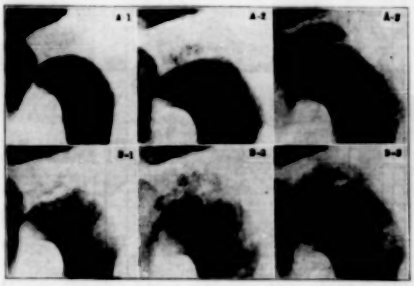

Fig. 3.—Dysgenesis of the femoral epiphysis in cretins under treatment. Different stages in ossification. Case A illustrates the fact that dysgenesis may occur while the patient is under treatment with thyroid. *A*, cretin, first treated at the age of 6 years; *A* 1, first appearance of calcification two and one half months after beginning treatment; *A* 2, five and one half months after beginning treatment; *A* 3, twenty-two months after beginning treatment. *B*, cretin, first treated at the age of 8 years and 9 months; *B* 1, before treatment; *B* 2, seven and one half months after beginning treatment; *B* 3, twelve months after beginning treatment.

It was found not only that those centers which were already calcified before treatment with thyroid was begun were affected but also that those centers whose ossification had been delayed developed in the characteristically abnormal manner, even after the institution of therapy.

Retardation and Defect in Development of the Brain.—When thyroid deficiency occurs in the early years of life it causes delay in the development of the brain. If the condition remains untreated permanent damage may result, and there may be histologic changes in the brain cells which have been described by Lotmar.[7] If treatment is instituted within the first year or two of life, permanent damage may at times be avoided and normal mental development may take place. If hypothyroidism does not occur until the later years of childhood, there may be no defect in the development of the brain and the intelligence quotient may be entirely normal, although the patient may be mentally sluggish and slow in response.

Diagnostic Significance of Structural Changes.—We have discussed so far the anatomic or structural changes brought about by hypothyroidism, especially those of the skeleton, and have pointed out that they are due principally to a retardation or a distortion of normal processes of development which occur during the growth period of early childhood. When all or most of these anatomic changes are combined, the clinical picture is usually unmistakable. However, some of these changes, for instance the dwarfing, the osseous retardation or the facial configuration, may occur in children who do not have hypothyroidism and may lead to mistaken

6. Wilkins, Lawson: Epiphysial Dysgenesis Associated with Hypothyroidism, Am. J. Dis. Child. **61**: 13 (Jan.) 1941.

7. Lotmar, F.: Histopathologische Befunde in Gehirnen von kongenitalem Myxodem (Thyreoplasie), Ztschr. f. d. ges. Neurol. u. Psychiat. **119**: 491, 1929; Entwicklungsstörungen in der Kleinhirnrinde beim endemischen Kretinismus, ibid. **136**: 412, 1931; Histopathologische Befunde in Gehirnen von endemischen Kretinismus, Thyreoplasie und Kachexia thyreopriva, ibid. **146**: 1, 1933.

diagnoses. If hypothyroidism exists, one should find not only anatomic changes but also definite physiologic evidences of diminished thyroid function, such as physical and mental sluggishness, circulatory changes and

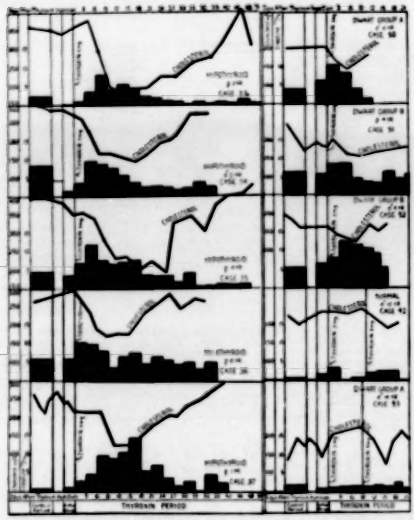

Fig. 4.—Response to a single dose of thyroxin. In the 5 patients with hypothyroidism (on the left side of the chart) there was a great and prolonged decrease in the serum cholesterol. In the 5 control patients presenting no evidences of hypothyroidism (on the right side of the chart) the decrease in the serum cholesterol was slight and transient. Dwarfs of group A showed noticeable retardation of caecus development, those of group B, normal caecus development.

metabolic and chemical abnormalities, which are discussed later.

The question now arises as to whether thyroid deficiency may occur during childhood without causing any of the characteristic structural changes. It is obvious that to cause such changes the deficiency must be present during the years of life in which the important developmental processes occur and that it must exist for a considerable period of time before any deviation from normal development becomes obvious. If hypothyroidism develops in a late period of childhood, for instance between the eighth and the twelfth year, when the more mature characteristics of the skeleton already have been attained, structural abnormalities are usually absent or of mild degree. If the deficiency is of only short duration, the deviation from normal may not be appreciable. In the first year of life the cretin is frequently hard to recognize by his appearance. Similarly, if hypothyroidism develops in a child at 6 years a number of years may elapse before there is sufficient deviation from normal development to suggest the diagnosis. Furthermore, if any thyroid treatment has been given during the important stages of development, all structural abnormalities may be prevented. Finally, it is theoretically possible that a mild degree of hypothyroidism might exist throughout childhood without causing characteristic anatomic changes. Since under the conditions mentioned thyroid deficiency might exist without any structural characteristics, the diagnosis of atypical or "borderline" forms of hypothyroidism or of mixed endocrine disturbances must depend on functional rather than structural changes.

FUNCTIONAL CHANGES

Mental sluggishness and physical inactivity are shown, to more or less degree, by all patients with hypothyroidism. The torpor and slow mental reactions characteristic of children with hypothyroidism are distinct from retarded or defective development of the brain. Thyroid therapy almost immediately causes the patient to become more alert and responsive; actual improvement in mental capacity occurs only gradually, and certain cerebral defects may be irreparable.

Diminution in the cardiac output and circulatory rate are constantly present. Clinically, however, the measurement of circulatory changes is difficult and unreliable in children. Although the pulse rate is usually decreased and the pulse pressure diminished, the difficulty of establishing true basal conditions and the absence of fixed norms make it impossible to apply the Read formula, which is the product of pulse rate and pulse pressure, to the diagnosis of hypothyroidism in children, as is sometimes done in adults. More reliable evidences of decreased peripheral circulation are a characteristic pale, grayish color of the cheeks and lips and a circulatory mottling of the skin. These are usually seen in children with hypothyroidism and, indeed, they are encountered with such regularity that one should hesitate to make a diagnosis of hypothyroidism in a child with bright, ruddy cheeks and lips. Whenever thyroid therapy is discontinued, the loss of color from the skin is usually the first evidence of a beginning relapse. A yellowish tinge of the skin due to the deposition of carotene is a more specific sign of hypothyroidism but is not found in all cases.

To devise more exact and objective methods of diagnosing thyroid deficiency the clinician has had to turn to laboratory methods. Although the study of the

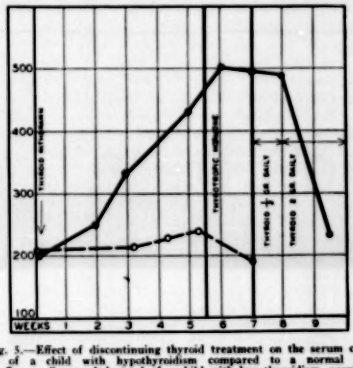

Fig. 5.—Effect of discontinuing thyroid treatment on the serum cholesterol of a child with hypothyroidism compared to a normal child. —●—●— = Serum cholesterol of a child with hypothyroidism, previously treated with 3 grains (0.2 Gm.) of desiccated thyroid daily. —o···o— = Serum cholesterol of a normal child who had received 5 grains (0.3 Gm.) of desiccated thyroid daily for one year previously.

metabolism of iodine might seem to be the most direct and specific approach to the problem, the technical difficulties of measuring the minute amounts of iodine present in the blood make it impractical for most laboratories. The methods of study which are readily avail-

able are the measurement of the basal metabolic rate, the serum cholesterol and the urinary excretion of creatine. We wish to discuss the recent work along these lines.

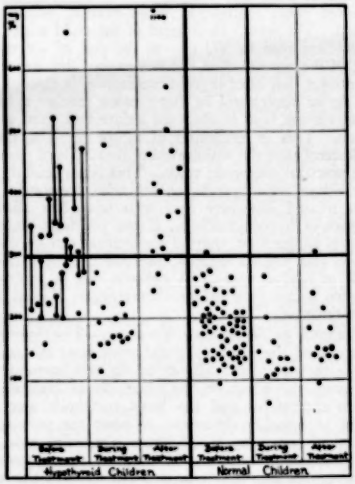

Fig. 6.—Serum cholesterol of children with hypothyroidism and of normal children before treatment, during treatment and after its withdrawal. Before treatment the concentration of cholesterol in children with hypothyroidism is often within the normal range. After treatment with thyroid is discontinued the cholesterol of children with hypothyroidism usually reaches high levels; that of normal children does not.

Basal Metabolism.—The measurement of the basal metabolic rate in young children or mentally subnormal children is unreliable, because of the difficulty in obtaining cooperation and establishing basal conditions. In only about one fourth of the children with hypothyroidism we [8] have studied could the basal metabolic rate be determined satisfactorily. In these cases the basal metabolic rates were — 25 per cent to — 40 per cent when compared to the Boothby-Sandiford surface area standards. When compared to these standards the rates of many obese children who present no evidences of hypothyroidism are just as low. However, when a comparison is made to the Talbot [9] height standards, children with hypothyroidism show definitely low metabolic rates, while obese children who do not have hypothyroidism have normal or even elevated rates. Occasionally we have seen children who have had a low basal metabolic rate even with the height standards and yet have presented no symptoms or signs whatever of thyroid deficiency. We do not believe that it is justifiable to base a diagnosis of hypothyroidism exclusively on the basal metabolic rate. The increasing popularity of the metabolism machine in the physician's office is becoming responsible for a growing number of ill considered diagnoses both in adult medicine and in pediatrics.

8. Wilkins, Lawson; Fleischmann, Walter, and Block, Walter: Studies on Hypothyroidism in Childhood: The Basal Metabolic Rate, Serum Cholesterol and Urinary Creatine Before Treatment, J. Clin. Endocrinol. **1**: 3 (Jan.) 1941.

9. Talbot, F. B.: Basal Metabolism Standards for Children, Am. J. Dis. Child. **55**: 455 (March) 1938.

Serum Cholesterol and Creatine Excretion in Untreated Hypothyroid Children.—The serum cholesterol can be determined accurately and simply by proper chemical methods without the use of a special diet. The determination of the excretion of creatine requires that the patient be given a diet low in creatine and that the urine be collected quantitatively and examined daily over a period of one to two weeks. The cholesterol and creatine of untreated children with hypothyroidism have been discussed by Wilkins, Fleischmann and Block.[8]

The serum cholesterol in the majority of children with hypothyroidism is between 250 and 600 mg. per hundred cubic centimeters, compared to a range of 100 to 300 mg. per hundred cubic centimeters in normal children. In the child with hypothyroidism the concentration of cholesterol from time to time may fluctuate as much as 200 mg. per hundred cubic centimeters, whereas we have not encountered fluctuations greater than 80 mg. per hundred cubic centimeters in normal children. At times we have found the serum cholesterol as low as 150 mg. per hundred cubic centimeters in children with severe hypothyroidism. Since the ranges of cholesterol found in normal patients and those with hypothyroidism overlap, a cholesterol value below 300 or 325 mg. per hundred cubic centimeters does not exclude thyroid deficiency, but a concentration above this is suggestive of this diagnosis, if other causes of hypercholesteremia, such as diabetes, nephrosis or hepatic disease, are not present.

There is a tendency for the excretion of creatine to be low in the child with hypothyroidism, although it may be as high as 4 mg. per kilogram of body weight daily. There are, however, great differences in the excretion of creatine in normal children, varying from 0.5 to 8 mg. per kilogram of body weight daily. It is therefore impossible to differentiate the untreated child with hypothyroidism from the normal child on the basis of the excretion of creatine. Likewise, we have not found that the creatine tolerance test is of diagnostic value.

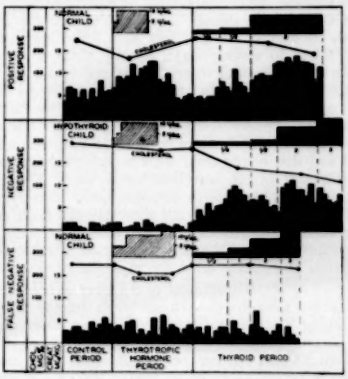

Fig. 7.—Response to thyrotropic hormone and to thyroid. The normal child having the "positive response" showed an increase of the excretion of creatine with thyrotropic hormone and with desiccated thyroid. The child with hypothyroidism having the "negative response" showed no increase of creatinuria with thyrotropic hormone but a definite increase with thyroid. The normal child having the "false negative response" showed no increase of creatinuria after the administration of either thyrotropic hormone or large doses of desiccated thyroid.

Sensitivity to a Standard Dose of Thyroxin Measured by the Effect on Serum Cholesterol and Urinary Creatine.—It has been pointed out frequently that a small dose of thyroid or thyroxin has a remarkable effect on a person with thyroid deficiency, while the same dose has slight if any effect on a normal person. Means [10]

TABLE 2.—*Effect of Thyrotropic Hormone and of Thyroid on Excretion of Creatine*

Type of Response	Increased Creatinuria with: Thyrotropic Hormone	Increased Creatinuria with: Thyroid	Children with Hypothyroidism	Normal Children	Dwarfs Without Hypothyroidism	Total
Positive	+	+	0	14	6	20
Negative	0	+	9	0	0	9
False negative	0	0	0	3	3	6
Totals			9	17	9	35

and his co-workers have emphasized that it is more important diagnostically to observe the effect on the basal metabolic rate of the administration of thyroid or the withdrawal of thyroid therapy than merely to measure the basal metabolic rate in the untreated patient. Since the determination of the basal metabolic rate is so unsatisfactory in children, Wilkins, Fleischmann and Block [11] decided to measure the serum cholesterol and the excretion of creatine in studying the effect of the administration and withdrawal of thyroid.

At first we attempted to compare the sensitivity of normal children and of those with hypothyroidism by giving small daily doses, ¼ grain (16 mg.) or ½ grain (32 mg.), of desiccated thyroid by mouth. Great differences between the two groups were found, especially in the effect on the excretion of creatine. Later we found that a more satisfactory differentiation could be made by giving a single intramuscular dose of 2 mg. or 5 mg. of thyroxin. Figure 4 shows the results of these studies. In the child with hypothyroidism a single dose of thyroxin causes a noticeable decrease in the serum cholesterol. The effect lasts for a long period, from thirty to seventy days, usually about forty days, before the cholesterol returns to its previous high level. In the normal child the same dose of thyroxin causes only a slight and transient lowering of the level of cholesterol, usually lasting no longer than ten days. Even when the cholesterol concentration of the normal child and that of the child with hypothyroidism are not far different before injection, as in cases 37 and 42 (fig. 4), the responses to thyroxin differ sharply. The excretion of creatine does not show as great a difference between the two groups of children, because some normal children (case 52) show a decided increase in the excretion of creatine after the injection of thyroxin.

Effect of the Withdrawal of Thyroid Medication on the Serum Cholesterol.—In studying the effect of discontinuing thyroid medication we [12] have observed that the serum cholesterol usually rises to high levels, between 300 and 600 mg. per hundred cubic centimeters, within a period of eight to twelve weeks. A similar rise of cholesterol does not occur in a normal child if thyroid is given for a period and then discontinued. This is illustrated in figure 5, in which are compared the cholesterol values of a normal child and one with hypothyroidism. Each had received large doses of thyroid for a long period. The concentration of cholesterol in each case was approximately 200 mg. per hundred cubic centimeters when thyroid was discontinued. The serum cholesterol of the child with hypothyroidism rose to 500 mg. at the end of six weeks; that of the normal child did not exceed 240 mg. It is of interest that after thyroid medication is discontinued the serum cholesterol in many cases reaches a higher concentration than is observed before treatment is first begun. This is illustrated in figure 6. The rise of cholesterol after the withdrawal of thyroid is of considerable practical diagnostic value. This is particularly true in children with hypothyroidism who previously have been treated elsewhere and who have lost all their stigmas of hypothyroidism. If the previous diagnosis is open to question, thyroid medication can be discontinued and the cholesterol observed over a period of eight to twelve weeks. A definite rise in cholesterol is often found long before characteristic clinical signs have returned.

Response to Thyrotropic Hormone.—The thyrotropic hormone of the pituitary gland stimulates the activity of the thyroid gland. By injecting this hormone and observing the effect on the excretion of creatine, the serum cholesterol and the basal metabolic rate, one might presumably determine whether the patient has a thyroid gland capable of functioning effectively. In studying this problem we [13] found that the excretion of creatine was the most sensitive indicator of the effect of medication with thyroid, because in normal children the administration of thyroid usually causes a definite increase in the output of creatine but has little effect on the serum cholesterol. In making the test, the average daily output of creatine was determined over a control period of one to two weeks. Thyrotropic hormone,[14] in doses of 5 to 10 units per kilogram of body weight, was injected daily for about ten days, and the daily excretion of creatine was measured. Treatment was then omitted until the excretion of creatine returned to the base level. Finally, the effect of desiccated

TABLE 3.—*Summary of Biochemical Studies*

	Hypothyroidism	No Hypothyroidism
Basal metabolic rate—before treatment		
Surface area standard	−10 to −40%	−10 to −28% (obesity)
Height standard	−14 to −32%	+40 to −15% (obesity)
Cholesterol—before treatment		
Range for group	150-600 mg. per 100 cc.	100-300 mg. per 100 cc.
Spontaneous fluctuations	200 mg. per 100 cc.	83 mg. per 100 cc.
Creatine—before treatment	0.0-3.8 mg. per Kg. per day	0.6-7.8 mg. per Kg. per day
Sensitivity to 5 mg. of thyroxin		
Cholesterol decrease	120-229 mg. per 100 cc.	0-76 mg. per 100 cc.
Average duration of effect	38 days	9 days
Withdrawal of thyroid treatment—cholesterol increase	98-411 mg. per 100 cc.	10-64 mg. per 100 cc.
Effect of thyrotropic hormone on output of creatine	Negative	Positive or "false negative"

10. Means, J. H.: The Thyroid and Its Diseases, Philadelphia, J. B. Lippincott Company, 1937.

11. Wilkins, Lawson; Fleischmann, Walter, and Block, Walter: Studies on Hypothyroidism in Childhood: Sensitivity to Thyroid Medication as Measured by the Serum Cholesterol and the Creatine Excretion, J. Clin. Endocrinol. **1**: 14 (Jan.) 1941.

12. Wilkins, Lawson, and Fleischmann, Walter: Studies on Hypothyroidism in Childhood: The Effect of Withdrawal of Thyroid Therapy Upon the Serum Cholesterol; Relationship of Cholesterol, Basal Metabolic Rate, Weight and Clinical Symptoms, J. Clin. Endocrinol. **1**: 91 (Feb.) 1941.

13. Wilkins, Lawson, and Fleischmann, Walter: Studies on Hypothyroidism in Childhood: The Creatine and Cholesterol Response to Thyrotropic Hormone, J. Clin. Endocrinol. **1**: 98 (Feb.) 1941.

14. The "thyrotropic factor" of Ayerst, McKenna and Harrison, containing 50 units per cubic centimeter, was used.

thyroid or of thyroxin was tested. This last step is essential in distinguishing "true negative" from "false negative" responses, as we shall explain later.

The three types of response, "positive," "negative" and "false negative," which were encountered are illustrated in figure 7, which shows studies made on 3 children—a dwarf with hypothyroidism, his normal twin sister and another normal control. In the first normal child the injection of thyrotropic hormone caused a definite increase in the excretion of creatine and a moderate decrease in the serum cholesterol. Desiccated thyroid caused a similar response. In the child with hypothyroidism, thyrotropic hormone had no effect on the creatine or cholesterol, while small doses of desiccated thyroid caused a decided increase in the output of creatine and a decrease in the serum cholesterol. This is a "true negative" response to the hormone, because the increased output of creatine with desiccated thyroid shows that the excretion of creatine is actually responsive to the effect of the thyroid. The other normal child showed the third type of response, which we have termed "false negative." In this case neither thyrotropic hormone nor the usual doses of thyroid had any effect on the excretion of creatine. Such a failure to respond to thyrotropic hormone cannot be interpreted as indicating that the thyroid gland is absent or unresponsive, because even the administration of thyroid caused no increase in the output of creatine.

Nine children with hypothyroidism whom we studied showed negative responses. Normal children and dwarfs presenting no evidences of thyroid deficiency usually gave positive responses, but a few showed the "false negative" response. Table 2 shows the results in 35 cases studied. It should be pointed out that under certain circumstances thyroid deficiency might be present in a patient having a positive response to thyrotropic hormone. This would occur if the gland was present and capable of stimulation but nevertheless was underfunctioning from some cause. We have encountered 1 such case not included in the table but discussed in the next section.

SUMMARY OF SPECIAL DIAGNOSTIC STUDIES

In table 3 are summarized the results of the special laboratory studies discussed. Exact criteria for the diagnosis of thyroid deficiency cannot yet be stated. We believe that the work discussed is only a beginning in the search for more specific and objective methods of measuring thyroid function. Among 42 children with hypothyroidism whom we have encountered in the last five years, most have presented characteristic clinical pictures of cretinism or of juvenile hypothyroidism. In such cases the elaborate biochemical studies described have served only to confirm diagnoses which were already fairly clearcut. During the same period we have seen 50 other dwarfs. In a few of these dwarfs of stocky build, the presence of noticeable retardation of osseous development and certain atypical anatomic features have suggested the possibility of the existence of a hypothyroid factor. In most of such cases the biochemical studies have failed to reveal evidences of thyroid deficiency. In other children coming under observation, studies such as we have described have been of value in excluding erroneous diagnoses of hypothyroidism based on the existence of a low basal metabolic rate or of a single anatomic peculiarity. Concerning the existence of mixed pituitary-thyroid deficiency we know little. So far we have studied only 1 patient who presented substantial evidence of a mixed deficiency. She was a sexually immature girl aged 20 years. Biopsy demonstrated that her thyroid gland was present but atrophic. There were definite clinical and biochemical evidences of hypothyroidism. The injection of thyrotropic hormone apparently caused a biochemical response consisting of a fall in the cholesterol level from 369 to 221 mg. per hundred cubic centimeters. However, intensive thyroid therapy over a period of five years has brought about no sexual maturation and no appreciable acceleration in the rate of growth, in spite of the fact that the epiphysial lines are not closed. We think that this is the only case in which we have demonstrated a definite thyroid deficiency which may be secondary to a pituitary deficiency.

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POSTMENOPAUSAL OSTEOPOROSIS

ITS CLINICAL FEATURES

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Our object in this paper is to point out the existence of postmenopausal osteoporosis and to describe its clinical features. Some metabolic data showing the effects of therapy with estrogens and other agents are incorporated in other papers.[1]

It will probably be well to start by explaining and defining the term "osteoporosis." Adult bone is normally subject to two continuous processes—formation and resorption. The mass of bone may be deficient either because resorption is too great (hyperparathyroidism with osteitis fibrosa generalisata) or because formation is too little (osteoporosis or osteomalacia). Formation of bone may be too little, furthermore, either because the osteoblasts do not lay down sufficient osseous matrix or because the matrix, once laid down, is not calcified. The former condition is osteoporosis; the latter, osteomalacia or rickets (fig. 1).

It is thought that stresses and strains are an important stimulus to osteoblastic activity and that the atrophy of disuse is due to a decrease of this stimulus. There is considerable evidence, furthermore, that the osteoblasts manufacture the enzyme phosphatase and that the serum phosphatase level (in the absence of hepatic disease) is an index to osteoblastic activity. An important clinical inference is based on these two suppositions. It may be stated as follows: In the presence of a rarefied skeleton, which is accordingly more subject to stresses and strains than the normal, the serum phosphatase level will be high unless the cause of the rarefaction is primary hypoplasia of the osteoblasts, i. e., osteoporosis. Hence a most important feature of osteoporosis is the absence of a raised phosphatase level.

Since osteoporosis is really not a disease of calcium metabolism, it is not surprising that the serum calcium and phosphorus levels are normal.[1a] The same is not

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1. Albright, Fuller; Bloomberg, Esther, and Smith, P. H.: Post-Menopausal Osteoporosis, Tr. A. Am. Physicians, to be published. Albright and Bloomberg.[2]

1a. An exception to this statement occurs when young individuals have a large proportion of their skeleton abruptly immobilized by infantile paralysis or by a cast; under these circumstances one may encounter a hypercalcemia. This will be the subject of a separate communication.

always true of the urinary excretion of calcium and phosphorus, probably for the following reason: Since normally some of the calcium and phosphorus which is set free by the process of resorption of bone is used again for formation of bone, it follows that any curtailment of the latter process would increase the excretion of calcium and phosphorus in the urine. However, once the skeleton has become extremely depleted, the amount of calcium and phosphorus derived from resorption of bone will be small even though the amount of resorption per unit of skeleton remains constant. When this situation has arisen the urinary excretion of calcium and phosphorus will be normal or even low. Hence hypercalciuria and hyperphosphaturia disappear after the skeleton becomes demineralized in osteoporosis, in contradistinction to hyperparathyroidism, in which they persist regardless of the degree of decalcification.

REVIEW OF THE LITERATURE

We are by no means the first to suggest a connection between ovarian function and calcium metabolism. Lawrence and Riddle [2] showed that there is more phosphorus in the blood stream of female than of male fowls and that still larger amounts of phosphorus are found in the blood of laying hens than of nonlaying hens. Riddle and Reinhart [3] demonstrated that there is a definite rise in the blood level of calcium in pigeons at the time the eggs are ready to leave the ovary. Hughes, Titus and Smits [4] showed an increase in serum calcium in laying hens. Macowan [5] correlated the degree of rise of the serum calcium level in the hen with the size of the egg. Riddle and Dotti [6] found in normal, hypophysectomized and thyroidectomized pigeons that the giving of follicle-stimulating hormone produces a rise in serum calcium; no similar rise was noted in castrate pigeons. Kyes and Potter [7] noted that the long bones of female pigeons are solid while those of male pigeons are filled with marrow. Gardner and Pfeiffer [8] gave estrogenic material to mice and noted that the marrow cavities were almost completely replaced by compact bone or by coarse bone spicules. Gardner and Pfeiffer [8] showed that the giving of testosterone hinders this effect of estrogen on the skeletons of mice. Pfeiffer and Gardner [9] found that administration of estrogen to pigeons causes hypercalcification of the long bones in both males and females and likewise raises the serum calcium level. Bach [10] administered estrogen to female rats and found that there is an initial fall in the excretion of calcium followed by an increased excretion.

ETIOLOGY OF OSTEOPOROSIS

Whereas it is our primary object in this paper to point out that the postmenopausal state is a factor in osteoporosis, it might be well first to discuss other factors or possible causes of this condition. Factors which have been suggested are disuse, dietary deficiency, gastric hypoacidity, repeated pregnancies, long-standing thyrotoxicosis, senescence and Cushing's disease.

The atrophy of disuse is a well recognized clinical entity. It is most often produced by immobilization in a plaster cast; it occurs in a limb which is affected by a flaccid paralysis. It is undoubtedly a factor in the generalized osteoporosis seen in older persons as their lives become more sedentary. An important differential clinical point is the fact that the atrophy of disuse seldom involves the skull, even when a patient is bedridden. This fact often helps to differentiate the condition from mild hyperparathyroidism but does not help to differentiate it from postmenopausal osteoporosis. In the series of cases studied in this paper (summarized in the accompanying table) an attempt has been made to call attention to any possible part played by the atrophy of disuse in the individual cases. In case 20, for example, the sequence of events may have been an automobile accident, the fracture of some vertebrae due to an adequate cause and the atrophy of other vertebrae due to immobilization. There is evidence, however, that atrophy due to forced disuse is greater in patients after the menopause than before (case 34).

We do not have any definite convictions as to what part diet may or may not play in the causation of osteoporosis. Diet, of course, has everything to do with osteomalacia, but that is an entirely different disease. There are at least three ways in which diet might be thought to play a part. Some investigators apparently believe that the increased availability of calcium and phosphorus in the system as the result of a diet rich in these substances is a stimulus to osteoblastic activity and that a decreased availability leads to decreased osteoblastic activity. As far as we are aware, there is no evidence to support this point of view. If the amount of calcium and phosphorus in the diet has any effect on the causation of osteoporosis, it seems unlikely that it is by such a mechanism. A second possibility is that an increased availability of calcium and phosphorus in the system because of the diet would decrease the amount of resorption of bone. If such were the case, any primary hypofunction of the osteoblasts would be partially offset by the decreased resorption and the patient would be benefited. Such a hypothesis would explain the apparently beneficial effect obtained by some investigators [11] in the treatment of patients with osteoporosis with diets high in calcium and phosphorus and large amounts of vitamin D. We favor the second possibility; it is in keeping with the concept which has been frequently emphasized from this clinic that a diet high in calcium and phosphates prevents the decalcification due to hyperparathyroidism. Finally, as a third possibility, a diet inadequate in protein might lead to a negative nitrogen balance, and this in turn might make it impossible for the osteoblasts to lay down the necessary organic matrix, which is the first step in the formation of bone. We believe that some of the osteopathies which have been attributed to a lack of calcium and phosphorus in the diet are really due to protein starvation.

In the table it will be noted that there were few abnormalities in the diet in this group of cases, and we are inclined to minimize the effect of diet.

Before the part played by diet is passed by, however, it might be of interest to discuss two recent papers by Prof. E. Meulengracht,[12] of Copenhagen. This author uses the terms osteomalacia and osteoporosis interchangeably. The cases described,

2. Lawrence, J. V., and Riddle, Oscar: Studies on the Physiology of Reproduction in Birds: VI. Sexual Differences in the Fat and Phosphorus Content of the Blood of Fowls, Am. J. Physiol. **41**: 430, 1916.

3. Riddle, O., and Reinhart, W. H.: Studies on Physiology of Reproduction in Birds: Blood Calcium Changes in Reproductive Cycle, Am. J. Physiol. **76**: 660, 1926.

4. Hughes, J. S.; Titus, R. W., and Smits, B. L.: Increase in Calcium of Hens' Blood Accompanying Egg Production, Science **65**: 264, 1927.

5. Macowan, M. M.: Observations on Ductless Glands, Serum Calcium and Egglaying in Fowl, Quart. J. Exper. Physiol. **21**: 383, 1932.

6. Riddle, O., and Dotti, L. B.: Blood Calcium in Relation to Anterior Pituitary and Sex Hormones, Science **84**: 557, 1936.

7. Kyes, P., and Potter, T. S.: Physiologic Marrow Ossification in Female Pigeons, Anat. Rec. **60**: 377, 1934.

8. Gardner, W. U., and Pfeiffer, C. A.: Skeletal Changes in Mice Receiving Estrogens, Proc. Soc. Exper. Biol. & Med. **27**: 678, 1938; footnote 20.

9. Pfeiffer, C. A., and Gardner, W. U.: Skeletal Changes and Blood Serum Calcium Level in Pigeons Receiving Estrogens, Endocrinology **23**: 485, 1938.

10. Bach, E.: Follikelhormon und Kalkstoffwechsel, Klin. Wchnschr. **16**: 230, 1937.

11. Bauer, Walter, and Marble, Alexander: Studies on the Mode of Action of Irradiated Ergosterol: II. Its Effects on the Calcium and Phosphorus Metabolism of Individuals with Calcium Deficiency Diseases, J. Clin. Investigation **11**: 1, 1932. Adams, M.; Boothby, W. M., and Snell, A. M.: Metabolic Studies in Osteoporosis, Am. J. Physiol. **114**: 383, 1936.

12. Meulengracht, E.: Osteomalacia of the Spinal Column from Deficient Diet or from Disease of the Digestive Tract: I. From Deficient Diet, Acta med. Scandinav. **101**: 138, 1939; II. Osteomalacia Achylica, ibid. **101**: 157, 1939.

however, are cases of what would be diagnosed in our clinic as "osteoporosis." The patients had normal serum calcium, phosphorus and phosphatase values. The disease was confined mostly to the spines. The first of these papers had to do with 6 patients in whom Meulengracht attributed the condition to faulty diet and the second paper with 9 patients in whom he attributed the condition to hypochylia, not necessarily achylia. Of these 15 patients, 11 were women who had passed through the menopause, and, in our opinion, they were probably suffering from postmenopausal osteoporosis. The osteoporosis of 1 of the men (case I) could be attributed just as well to the atrophy of disuse. The first symptom was a nocturnal epileptic attack which led to paralysis of the legs and caused the patient to be bedridden for a few weeks. It is common to fracture a perfectly normal vertebra in an epileptic attack,[13] and the immobilization due to the fracture would then lead to osteoporosis. The osteoporosis of the second male patient (case III) was less convincing than that of the female patients. Thus the statement was made that "there was calcium deficiency of the vertebrae, but not very pronounced." The third male patient (case XIV) entered the hospital with severe scurvy. The vitamin C deficiency in itself might have been a factor in the osseous disease. The roentgenograms did show definitely increased radiability of the vertebrae. The statement was made, however, that the anterior longitudinal ligaments were considerably ossified. It would be our opinion that this indicated that the patient was suffering from or had suffered from spondylitis, which is probably akin to rheumatoid arthritis, and that the atrophy was due to this condition. We have recently studied a similar case in which there were increased radiability of the vertebrae and calcification of the anterior longitudinal ligaments. This case was not included in the series here analyzed because there seemed to be a definite local cause for the disease of the bone. Meulengracht's case XV (the fourth male patient) was complicated. There was a twenty year history of dyspepsia at the end of which time a pyloric resection was done for pyloric stenosis due to a gastric ulcer. There was increased radiability of the spine, which almost surely was related to the gastrointestinal history. It would appear to us, therefore, that of these 15 cases 11 were probably postmenopausal osteoporosis and that the remaining 4 in men could easily be explained on other grounds. That diet or gastric hypoacidity was an important factor seems inadequately established although by no means disproved. The possibility remains that the prerequisites for the development of the disease are the postmenopausal state plus an inadequate diet.

Repeated pregnancies probably cause a drain on the body's supply of calcium and constitute a well known factor in the causation of osteomalacia. However, it is unlikely that pregnancy would have any effect on the causation of osteoporosis. It was considered, however, of interest to list in the table the number of pregnancies in the various cases.

There is an increased excretion of calcium in the urine and feces in cases of thyrotoxicosis.[14] Williams and Morgan[15] presented some evidence that long-standing thyrotoxicosis leads to increased radiability of the skeleton.

It is perhaps of interest that all of their 7 patients were women, and, as was pointed out by them, that

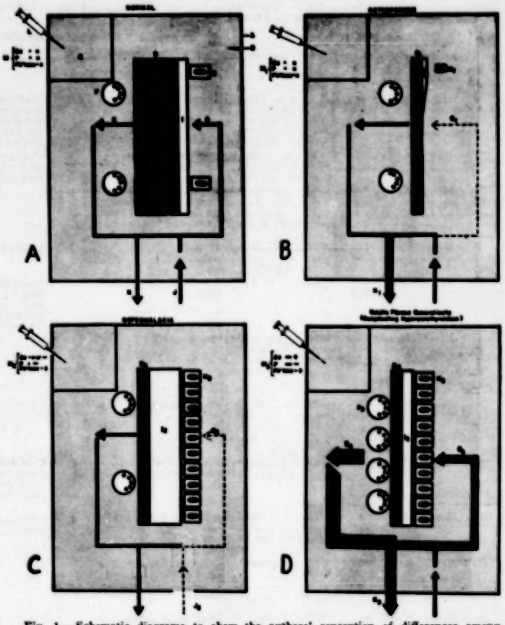

Fig. 1.—Schematic diagrams to show the authors' conception of differences among normal function of bone, osteoporosis, hyperparathyroidism with osteitis fibrosa generalisata and osteomalacia. *A*, body limits; *B*, body fluids; *C*, body serum, a compartment of fluid easy to tap for analysis; *D*, mass of bone with two surfaces, one at which bone is being resorbed and one at which it is being laid down; *E*, arrow indicating by its size the rate of resorption of calcium and phosphorus; *F*, osteoclast; *G*, rate of deposition of calcium and phosphorus; *H*, osteoblast laying down osteoid (*I*); *J*, calcium and phosphorus entering the body from the gastrointestinal tract; *K*, calcium and phosphorus leaving the body by the kidneys or by other exits; *L*, syringe obtaining serum for analysis, and *M*, blood values (n = normal, + = high and — = low).

A. *Normal.*—Note that the calcium and phosphorus going into bone equals that coming out of bone and that part of that which comes out goes back in.

B. *Osteoporosis.*—Note decreases in the mass of bone (D_3); primary hypoplasia of osteoblasts (H_3); decreased deposition of osteoid (I_3); decreased deposition of calcium and phosphorus (G_3); increased excretion of calcium and phosphorus (K_3), and normal blood values (M_3).

C. *Osteomalacia.*—Note decreased mass of bone (D_2); hyperplasia of osteoblasts because of increased stresses and strains (H_2); increased deposition of osteoid which is inadequately calcified because of serum calcium and phosphorus values; decreased deposition of calcium and phosphorus (G_2); primary difficulty in absorbing calcium and phosphorus from the gastrointestinal tract (J_2), and abnormal blood values (calcium normal or low, phosphorus low and phosphatase high).

D. *Osteitis Fibrosa Generalisata Complicating Hyperparathyroidism.*—Note increased excretion of calcium and phosphorus in the urine (K_3); increased resorption of calcium and phosphorus (E_3) increase of osteoclasts (F_3); decreased mass of bone (D_3); increased formation of bone by osteoblasts (I_3) because of increased stresses and strains; increased deposition of calcium and phosphorus (G_3) because serum is not undersaturated in respect to calcium phosphate (i. e. the serum calcium level is sufficiently high almost to offset the low serum phosphorus content), and the high phosphatase level (M_3).

5 were over the age of 50. We are not aware that histologic studies have been done on osseous material from patients with thyrotoxicosis, and the nature of the disease of bone is still unknown. Patients 38, 39 and 40[16] in the series here reported had a history of thyrotoxicosis. The osseous changes were similar from

13. Palmer, H. A.: Vertebral Fractures Complicating Convulsive Therapy, Lancet **2**: 181, 1939.

14. Aub, J. C.; Bauer, Walter; Heath, C., and Ropes, M.: Studies of Calcium and Phosphorus Metabolism: III. The Effects of the Thyroid Hormone and Thyroid Disease, J. Clin. Investigation **7**: 97, 1929. Pugsley, L. I., and Anderson, E.: The Effect of Desiccated Thyroid, Irradiated Ergosterol and Ammonium Chloride on the Excretion of Calcium in Rats, Biochem. J. **28**: 754, 1934. Puppel, I. D., and Curtis, G. M.: Calcium and Iodine Metabolism in Thyroid Disease, Arch. Int. Med. **58**: 957 (Dec.) 1936.

15. Williams, R. H., and Morgan, H. J.: Thyrotoxic Osteoporosis, Internat. Clin. **2**: 49, 1940.

16. Case 40 was previously reported as case 383 by J. H. Means (The Thyroid and Its Diseases, Philadelphia, J. B. Lippincott Company, 1937).

Summary of Clinical Observations

Identification		Age and Time Data			Etiology			Symptomatology		
Case	Patient	Age and Date When Seen	Age at Menopause	Interval Between Menopause and First Symptom, Years	Diet	Number of Pregnancies	Evidence for Disuse Atrophy as a Factor	First Symptom and Precipitating Incident	Duration of Symptoms *	Disability
AFTER PHYSIOLOGIC MENOPAUSE										
1	Miss L. M.	65 1935	47	10	Generally poor; little milk until 7 yrs. before; 1 glass daily since	0	0	Fractured surgical neck of humerus in a fall	1 day	Fracture not united
2	Mrs. F. T.	65 1931	50	14	Drank milk	2	Inactive since fracture of 2 mos. duration; cast for 2 mos., then limited activity	Spontaneous fracture of both bones of lower right leg, without adequate trauma	1¼	Unable to do housework for 2 years
3	Miss P. S.	65 1937	51	9	Little milk; meat once daily	0	Change from active to sedentary occupation	Spine "gave way" while pushing boat off dock; pain in lower back since	5	Feels insecure; cane, corset and brace
4	Miss E. F.	65 1904	35	31	½ pint milk daily for 30 yrs. before menopause; for next 19 yrs. 1 pint daily as beverage; once daily all her life	0	0	Pain in right iliac region following jolt in car	3 mos.	..
5	Mrs. D. S.	64 1902	40	24	No data	5	Limited activity	Pain in legs with increasing weakness	4 mos.	Insecure
6	Mrs. M. M.	63 1934	52	9	Rarely ate meat; no milk	1	Bedridden for 3 wks. 1 yr. before seen; back strapped for 6 mos. thereafter	Continuous burning pain in back, arms and legs since "throwing brake" on car	2	Requires rest periods; corset and brace
7	Mrs. W. R.	63 1935	54	8	Drank no milk	5	0	Onset of severe pain in back while pounding tacks in footstool; had both weakness and pain on motion thereafter	1	Limited activity; corset and brace
8	Mrs. I. E.	63 1905	38	10	See "Comment"			Radiating pain in abdomen and back, thought to be arthritis; no precipitating incident	3 mos.	Corset and brace
9	Miss I. M.	62 1937	..	..	Some milk as a beverage for 5 yrs.	0	Cast for ankle 3 mos.; crutches for 2 mos. in addition	Slipped on steps and fractured ankle; later had pain in hips and lower part of back, especially on lying down	2	Walking painful; especially climbing stairs
10	Mrs. H. K.	62 1937	50	11	Milk in cooking, not as beverage; occasionally cottage cheese	4	Immobilization, 16 wks.	Fractured hip from fall on rug	1½	Fracture not united
11	Mrs. A. McD.	61 1939	47	13	1 glass to 1 pint milk daily as beverage and in cooking; no cottage cheese	0	0	Onset of sudden severe pain in right flank while sitting in church; numbness in left leg	5 mos.	Requires rest periods, care; corset and brace
12	Mrs. E. H.	60 1908	45	15	Little meat; a few vegetables and some butter; carbohydrates	3	0	Sudden pain in back on leaning forward	2 mos.	0
13	Mrs. E. P.	60 1939	53	6	Whole milk in cooking; cream in coffee and on cereal; no cottage cheese	..	Bedridden since injury	Pain in back since fall down six steps; landing in sitting position	1½	Bed most of the time; cane, corset and brace
14	Mrs. S. F.	59 1933	49	9	Always drank 1 glass of milk daily	2	0	Onset of sudden severe pain in left scapula while stooping forward	1	Generalized weakness
15	Mrs. F. H.	59 1933	48	10	Used milk in cooking only; ate meat and vegetables	5	0	Hit by trolley car; pain in back thereafter	1	..
16	Mrs. I. H.	59 1936	38	9	No milk	6	0	Fell on ice; entered hospital at once for pain in back	1 day	Pain and spasm; corset and brace
17	Mrs. R. C.	59 1936	38	14	No milk or cheese	2	0	Experienced "crack" in back on bending over; backache thereafter	7	Corset and brace
18	Mrs. D. G.	58 1932	50	7	No milk	2	Cast for 2 mos.; bedridden for 6 mos. because of fractured hip	Fell from street car and fractured hip; nonunion of fracture	9 mos.	Limp due to short left leg; corset and brace
19	Miss J. M.	57 1933	53	4	Moderate use of milk before menopause	0	0	Bent over and suffered sudden pain in back which persisted	1 wk.	Walks with cane
20	Miss M. M.	56 1937	48	7	No milk	0	0	Severe pain in left leg after fall on ice	1	Difficulty in walking, weakness; corset and brace
21	Mrs. M. W.	55 1934	44	11	No data	0	0	Fell on steps, striking knee and spine; severe back pain	1 day	0
22	Miss S. McA.	55 1939	45	7	Ate meat twice daily 10 yrs. before menopause, cottage cheese occasionally; 1 glass milk daily after menopause and more cheese in diet	0	Cast for 7 wks. for injury of back	Pain in back after severe jolt in car	3	Corset and brace

* The duration of symptoms is in years unless stated otherwise.

in Forty-Two Cases of Osteoporosis

Roentgenographic Study					Serum Chemistry				
Spine		Increased Radiability of Other Bones							
Increased Radiability	Deformed Vertebrae	Pelvis	Skull	Long Bones	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Phosphatase, Bodansky Units per 100 Cc.	Protein, Gm. per 100 Cc.	Comment; Associated Diseases
AFTER PHYSIOLOGIC MENOPAUSE									
+++	Ninth dorsal	++	—	++	9.6	3.6	3.0	6.4	Psychoneurosis; poor dietary habits for years
++	Multiple dorsal and lumbar	+++	—	—	10.1	3.1	...	7.2	Herpes zoster at 64; calcification of abdominal aorta; tuberculosis (old) of left knee causing spontaneous fracture; lower right tibia and fibula fractured without known trauma; died of pulmonary infarct
++++	Multiple middle lumbar and lower dorsal	0	+	0	10.4	3.6	4.8	5.9	Renal colic at 55 and 65; bilateral mastectomy for cystic mastitis; hypertension; gastric analysis; no free acid
++	First lumbar	—	—	—	10.6	4.4	...	...	In right kidney: hydronephrosis 1934; renal stone discovered 1 month after patient was placed in cast for fractured first lumbar vertebra in February 1935; later, nephrectomy
++	Multiple	+	+	—	10.5	3.6	...	...	Chronic cholecystitis; hypertension; unilateral oophorectomy 9 years after menopause for ovarian disease
++	Tenth and eleventh dorsal; first and second lumbar	—	++	+++	10.3	3.9	3.6	...	
+++	Multiple dorsal	+++	0	0	10.5	3.4	3.2	6.6	Gravel in urine at 55; mastectomy for cystic mastitis at 62; calcification of arteries; nontoxic nodular thyroid; amebic dysentery at 48 and 49
+++	Multiple dorsal and lumbar	+++	—	—	11.0	3.8	4.6	5.8	Typhoid in adolescence; "arthritis" since 48; hypertension; frequent attacks of gastrointestinal disorder, acute for 9 months; atony of the colon
+++	0	+++	—	+ See "comment"	....	4.4	3.5	6.0	Hypertension; left sacroiliac strain; right dorsal scoliosis
+	0	++	0	—	9.9	3.8	...	7.2	Gallstones and bilateral renal stones discovered while in traction 16 weeks for fracture; typhoid at 15 with gallstone colic; unable to walk for 2 years after typhoid
+++	Multiple	+++	0	+	10.9	3.2	4.1	5.7	Chordotomy for root pain; incontinence since
+++	Eleventh and twelfth dorsal; first lumbar	++	0	—	10.8	3.3	4.9	...	
+++	Seventh, ninth and twelfth dorsal; first lumbar	++	0	+	10.1	3.5	3.7	7.6	Dorsal kyphosis; cholelithiasis
+++	Multiple	+++	0	+	10.9	3.3	2.4	...	Calcification of aortic arch
+++	Twelfth dorsal; first, second and third lumbar	—	+	—	10.0	3.6	4.4	7.1	Arteriosclerosis, essential hypertension; pyelitis, asthma at 29
+++	Lower dorsal and first and third lumbar	++	0	0	10.1	3.7	4.4	5.7	Hypertrophic arthritis of hands; thyroid nodule (?)
++++	Twelfth dorsal and first lumbar	—	0	+	9.5	4.0	3.3	6.1	Heberden's nodes; kyphosis
++++	Eleventh dorsal	—	—	—	11.0	4.3	...	...	"Sour stomach"
++	Twelfth dorsal	++	0	0	11.7	4.0	...	...	Arteriosclerotic heart disease and arteriosclerosis; typhoid at 23; multiple sclerosis (?)
+++	Eleventh dorsal	+++	0	0	10.7	4.0	3.6	6.2	Actual cause of symptoms may have been ruptured disk rather than osteoporosis; arteriosclerosis ++; neuritis of left sciatic and femoral nerve
+++	First lumbar	+++	—	0	10.8	3.4	3.6	...	Fractured surgical neck of humerus at 50; asymptomatic syphilis at 19, Wassermann weakly positive
+++	Multiple dorsal and lumbar	..	—	—	9.3	3.5	2.9	...	Typhoid at 35; history of gastric ulcer

Summary of Clinical Observations in

Identification		Age and Time Data			Etiology			Symptomatology		
Case	Patient	Age and Date When Seen	Age at Menopause	Interval Between Menopause and First Symptom, Years	Diet	Number of Pregnancies	Evidence for Disuse Atrophy as a Factor	First Symptom and Precipitating Incident	Duration of Symptoms	Disability
23	Mrs. M. F.	54 1939	51	2	No milk	3	..	Fell on left side, turned ankle and wrenched back; later, pains radiating from spine	2	Legs weak; fatigues easily
24	Mrs. E. D.	49 1931	38	7	Normal diet but did not care for milk until 1931; milk and cheese continuously since	3	0	Gradual onset of Pain in back brought on by change in position	2	Corset and brace
25	Mrs. I. B. T.	49 1938	46	3	1 glass milk every other day before 1938; 3 glasses milk daily since	No data	0	Pain in back on bending over	3 mos.	0
26	Mrs. R. F.	49 1937	41	3	No milk	1	0	Pain in shoulders and back	3	Corset and brace
27	Mrs. K. M.	47 1932	40	6	Little calcium in diet	2	0	Vague skeletal pains	..	0
					AFTER ARTIFICIAL MENOPAUSE					
28	Mrs. M. S.	64 1940	41	14	2 glasses of milk a week as beverage	8	0	Shortening stature and rounding of back, with pain	9	Corset and brace
29	Mrs. M. G.	61 1936	33	28	No milk	6	..	Severe pain in lower part of back on closing upper sash of window	2	Lumbosacral portion of spine rigid
30	Miss A. T.	62 1935	43	19	No milk, meat or eggs	0	Has used crutches or cane since fracture of femur at 56	Severe back pain on motion since fall backward after tripping over rug	1 mo.	..
31	Miss E. S.	60 1936	32	21	Moderate amount of milk on cereal and in cooking; has eaten meat and varied diet all her life	0	Almost bedridden for 7 yrs; cannot walk alone	.....	7	Depends on crutches; teaches dress design sitting
32	Mrs. A. R.	58 1935	45	10	1 glass milk daily as beverage; milk in cooking; cheese frequently; high calcium and protein diet since 53	5	Changed to sedentary work at 54	Onset of severe pain between the shoulders while trying to raise upper sash of a window	4	Cautious activity with corset and brace
33	Miss I. S.	53 1938	52	10 mos.	No milk	0	0	Pain in knees, hips and lower part of back; pain in left shoulder	1 day	0
34	Miss T. M.	51 1938	33	15	Drinks little milk	0	Confined to bed 3 mos. at 33 after oophorectomy	Turned ankle and injured knee cartilage; pain and swelling of knee	5	Crutches, plaster cast on right knee
35	Mrs. C. DeN.	51 1940	36	13	A little milk used in coffee only before menopause; meat usually once daily	3	0	Pain in left sacroiliac region	2	Limitation of motion on bending backward
36	Mrs. M. B.	49 1938	28	14	Always 1 glass milk daily as beverage; occasionally cheese; always ate meat and vegetables; 1 pint milk daily since 1938	2	..	Sudden onset of pain in right shoulder and limitation of motion while driving automobile	2	Limited shoulder motion
37	Mrs. F. F.	42 1938	41	9 mos.	Daily milk 1934-1937; occasionally cheese	0	..	Gradual onset of back pain with increasing dorsal kyphosis; no precipitating cause	1	Active but uses corset and brace
					COMPLICATED BY HYPERTHYROIDISM					
38	Mrs. A. L.	60 1932	50	..	No use of milk; occasional use of cheese all her life	4	..	Gradual onset; no symptoms attributable to osteoporosis	..	Lateral curvature; corset and brace
39	Mrs. H. R.	60 1936	45	..	3 glasses milk a day up to age 20; 4-6 oz. cottage cheese; since menopause, 1 glass milk as beverage, 1 oz. cottage cheese daily	1	..	Symptoms of osteoporosis not complained of; marked by other symptoms	..	Limited activity; corset and brace
40[16]	Mrs. B. S.	50 1931	..	..	Low calcium and protein diet until 50, when first under care	0	..	Sudden onset of knifelike pain in lumbar region while driving automobile	3 mos.	Little activity; corset and brace
					MEN					
41	Mr. V. S.	60 1935	..	..	No milk	..	Changed to sedentary occupation 8 yrs. before	Symptoms probably not attributable to osteoporosis	2	Legs weak; uses cane; spastic gait
42	Mr. H. B.	48 1939	..	..	No milk or cheese	..	..	Experienced sharp pain and heard snap in region of twelfth dorsal vertebra after twist of back while playing golf	3	Ambles along with cane; bent over; wears brace

Forty-Two Cases of Osteoporosis—Continued

Roentgenographic Study					Serum Chemistry				
Spine		Increased Radiability of Other Bones							
Increased Radiability	Deformed Vertebrae	Pelvis	Skull	Long Bones	Calcium, Mg. per 100 Cc.	Phosphorus, Mg. per 100 Cc.	Phosphatase, Bodansky Units per 100 Cc.	Protein, Gm. per 100 Cc.	Comment; Associated Diseases
+++	Tenth dorsal; first, third, fourth and fifth lumbar	++	0	+	10.1	3.3	5.1	7.3	Area of Paget's disease of left side of ilium; calcification of abdominal aorta
+++	Multiple	+++	+	+	10.5	3.2	6.2	...	Calcification of aorta; operation for chronic cystic mastitis; symptomatic improvement after changes in diet
+++	0	—	+	—	10.6	3.2	4.1	...	Dorsal kyphosis; lower dorsal scoliosis
+	Multiple	+	—	0	11.0	4.2	...	...	Stone in left kidney (?); kyphosis
++	Lumbar	+	+	+	10.3	3.1	2.3	...	Osteitis fibrosa localisata of left radius; diagnosed after traumatic fracture; hyperparathyroidism ruled out; cholecystectomy at 46
					AFTER ARTIFICIAL MENOPAUSE				
+++	Multiple dorsal	—	0	+++	11.5	2.8	6.7	...	Syphilis of at least 11 years' duration; at least 5 pregnancies terminated in abortions
+++	Sixth, seventh and ninth dorsal; first and fifth lumbar	+++	0	+	10.6	3.5	3.6	...	Mushroom deformity of both wrists; absence of styloid process; old thoracic goiter
++++	First, third, fourth and fifth lumbar	++++	0	++	9.3	4.4	5.9	6.0	Hysterectomy and bilateral oophorectomy at 43; gastric ulcer at 56; ununited fracture of femur at 56; hypertension; aortic calcification
+++	Second, sixth, ninth, eleventh and twelfth dorsal	+++	—	+++	10.4	3.7	4.0	7.8	Bilateral oophorectomy at 32; cystic ovaries; fractured arm at 54; typhoid at 25; aortic calcification
+++	Multiple dorsal and first lumbar	+++	+	0	10.1	3.0	3.7	6.3	Radium treatment for fibroid tumors at 45; typhoid at 17
++	0	+	—	+	11.3	3.9	4.5	7.6	Bilateral oophorectomy at 52
++	0	++	+	+++	10.0	3.6	4.5	4.9	Menopause at 33 after operation for uterine fibroid; hot flashes have persisted ever since; a total of more than 35 rib fractures; multiple fractures and sprains of legs and feet and ankle (especially dense end plates on vertebral bodies)
+	0	+	—	—	11.1	4.0	5.6	7.6	Bilateral oophorectomy at 36; indication not known
++	First and second lumbar	++	—	+	10.8	3.6	3.6	...	Bilateral oophorectomy at 28; hysterectomy at 32; subachromial bursitis
+++	Multiple lumbar and dorsal	+	0	0	10.5	4.2	3.6	7.3	Oophorectomy at 41 for endometriosis; operation followed by nocturnal seizures, exact nature of which has not been determined
					COMPLICATED BY HYPERTHYROIDISM				
++	0	—	—	—	9.3	3.8	...	...	Operation for severe hyperthyroidism December 1932; mild diabetes mellitus; arteriosclerosis
++	0	+	—	—	10.1	4.6	3.3	...	Subtotal thyroidectomy for hyperthyroidism, 1936; aortic calcification
+++	First and fifth lumbar	+++	0	+	10.5	3.5	3.0	7.0	Thyroidectomy at 41 (1922) for long-standing exophthalmic goiter (12 yrs.); slight residual thyrotoxicosis thereafter; arteriosclerosis; hypertensive heart disease; congestive failure
					MEN				
++	Seventh and ninth dorsal; first and fifth lumbar	++	0	+	10.3	4.0	2.4	...	Rickets as a child, requiring use of brace; hypertrophic arthritis
++++	Multiple dorsal and lumbar	++++	+	+	10.5	3.2	3.6	6.7	Coronary thrombosis at 43; calculus in left kidney at 46; in right kidney one month later

a clinical point of view to those seen in typical postmenopausal osteoporosis.

All 3 of these patients were women who had experienced the menopause. It is believed that the menopause alone could have accounted for all the osseous changes. Whether the thyrotoxicosis was an associated factor or the only factor cannot be stated.

Fig. 2 (case 13 in table).—Crushed vertebra.

The bones, like so many other tissues (skin, hair, elastic tissue) atrophy in old age in both sexes. Fracture of the hips of very old people is a common clinical manifestation of this process. This atrophy is osteoporosis and is generally designated "senile osteoporosis." In the group of cases here reported we were not concerned with senile osteoporosis, and we have arbitrarily omitted all cases of osteoporosis occurring after the age of 65.

Since the osteoporosis of Cushing's syndrome is probably closely related to that occurring after the menopause, it will be discussed after menopausal osteoporosis.

CLINICAL CHARACTERISTICS OF POSTMENOPAUSAL OSTEOPOROSIS

Some clinical data on 42 cases of osteoporosis are tabulated. The chief argument for the existence of postmenopausal osteoporosis, other than the beneficial effects of estrogen on the calcium metabolism [17] in these cases, is the frequency with which osteoporosis occurs in women after the menopause. Thus the 42 cases listed in the table represent all the cases of generalized osteoporosis without an obvious cause, such as infantile paralysis, which have come to our attention or which we have been able to find in the hospital diagnosis index since the year 1931. Patients over 65 years of age have been excluded because of the possibility of senescence as a factor (as noted previously). By the term "generalized osteoporosis" it is not implied that the osteoporosis involves all the bones of the body but that it is not confined to a local region such as one vertebra or one extremity.

Of the 42 patients, 40 were women who had passed the menopause. Two were men (cases 41 and 42); no explanation for the osteoporosis of these was apparent. In no instance did the condition occur in women before the menopause. That this is not just a matter of age is not entirely disposed of by the 10 women in whom osteoporosis occurred with artificial menopause, since the ages of these 10 women were not strikingly different from those in the group of patients with physiologic menopause. Case 36 was interesting, however, in this connection in that the patient underwent an artificial menopause at the age of 28 and her symptoms developed at the age of 42. The average time of onset of symptoms after the menopause was nine and one-half years in the 27 cases of uncomplicated physiologic menopause and thirteen and two-fifths years in the 10 cases of artificial menopause. The difference between these two values is not statistically significant.

It will be seen from the table that postmenopausal osteoporosis has a predilection for the spine and the pelvis; long bones are involved only in the cases of more severe involvement. The skull is notable for its lack of involvement; this is an important point in differentiating postmenopausal osteoporosis from hyperparathyroidism, since in the latter condition the skull is one of the first bones to show roentgen evidence of involvement. The spinal lesions consisted of fractured or crushed vertebrae (fig. 2), the so-called fish vertebrae (fig. 3) and herniation of the nucleus pulposus through the end plates of the vertebrae, or "schmorlsche knoetchen" (fig. 4).

Fig. 3 (case 24 in table).—So-called fish vertebra. Note that intervertebral disks have expanded into vertebrae, converting them into biconcave disks.

The commonest syndrome is that due to a vertebral lesion. Essentially the same story keeps repeating itself: A woman, about ten years after the menopause, receives a minor jolt (by going over a bump in an automobile, for example); she experiences a pain in the back; finally she has a roentgen examination which reveals the condition. This examination may be made for some other malady, and in these instances there may be no symptoms. Since, as previously discussed, there is an increased excretion of calcium in the urine in the early stages of osteoporosis, it is not surprising that some patients with this condition have urinary calculi. Patient 7,

17. Albright, Fuller, and Bloomberg, Esther, to be published.

for example, noted the passing of gravel on frequent occasions for one year after the menopause, which occurred at the age of 54. There were then no further symptoms until nine years later, when she experienced a severe pain in the back while pounding some tacks into a footstool. Patients 3, 4, 10 and 26 also had histories of urinary calculi (as did patient 42, one of the two men in the series). On physical examination patients with osteoporosis tend to show their age prematurely. Their skin is noticeably thin, this condition suggesting that the atrophy is more widespread than just in the bone matrix.

CUSHING'S DISEASE

The pathologic condition of bone associated with Cushing's disease is osteoporosis and has many of the clinical characteristics of postmenopausal osteoporosis. We have studied 5 patients (2 with adrenal cancers and 3 without) who will be the subject of a separate report.[18] In this disease there is a decrease or an absence of the formation of estrogen and, in addition, an increase in urinary androgens.[19] It is interesting that Gardner and Pfeiffer [20] have found that testosterone inhibits the effect of estrogen on the formation of bone in doves, and it may be that the excessive androgens in Cushing's disease cause the osteoporosis to be so severe. It may be partly for this reason, too, that we have found estrogen ineffective in Cushing's disease in producing a positive calcium balance.[18] However, in our opinion,[21] the most important factor in the causation of the osteoporosis in Cushing's disease is the negative nitrogen balance due to an increased conversion of protein into sugars.

MENOPAUSAL OSTEOPOROSIS COMPLICATED BY PAGET'S DISEASE

Case 23 in the table is of much theoretical interest in that postmenopausal osteoporosis was superimposed on Paget's disease. The net result was what one would have expected. It is the belief of one of us (F. A.) from unpublished data that the sequence of events in Paget's disease is (*a*) destruction of bone due to an unknown cause, (*b*) osteoblastic stimulation due to increased stresses and strains and (*c*) overgrowth of bone and increase of the serum phosphatase level as a result of osteoblastic stimulation. Thus if Paget's disease were superimposed on osteoporosis one would expect steps *b* and *c* to be missing because of the primary hypofunction of the osteoblasts. Patient 23 had a normal phosphatase level, and the roentgenogram showed any evidence of overgrowth of bone in the area of Paget's disease to be lacking.

Another example of the two conditions occurring in the same patient was recently seen (Mrs. M. L.). The patient was 62 years of age and had had a physiologic menopause at the age of 44. She had been under treatment for pernicious anemia for four years. She had advanced atrophy of the skin and had had a vulvectomy for kraurosis. There was advanced osteoporosis of the spine and pelvis, but no fractures of the vertebrae. The extraordinary feature of the case, however, was the patient's skull. The whole top of the head was flat and soft, and the pulsations of the brain could be felt and seen. The roentgenogram showed extreme decalcification of the skull due to Paget's disease. Here again steps *b* and *c* were left out, in all probability because

Fig. 4 (case 13 in table).—Herniation of nucleus pulposus through end plate of vertebra ("schmorlsche knoetchen").

of superimposed postmenopausal osteoporosis. The patient's serum calcium was 9 mg., serum phosphorus 3.2 mg. and serum phosphatase 15.7 and 21.9 Bodansky units per hundred cubic centimeters.

POSTMENOPAUSAL OSTEOPOROSIS COMPLICATED BY HYPERPARATHYROIDISM

In a previous publication from this clinic [22] a case was described in which the combination of osteoporosis with hyperparathyroidism was present. Hyperparathyroidism when it does cause disease of bone does so by increasing destruction of bone. Normally this process is partially met by increased repair of bone due to osteoblastic activity, and the phosphatase level is high. If the condition is complicated by osteoporosis the osseous changes will be out of proportion to the degree and the duration of the hyperparathyroidism, and the phosphatase level will be unexpectedly low for the degree of decalcification.

SUMMARY AND CONCLUSIONS

1. Calcium deficiencies of the skeleton due to metabolic disorders are divided into those due to increased resorption of bone and those due to decreased formation of bone; deficiencies due to decreased formation of bone are further subdivided into those in which calcium is not deposited in osteoid tissue (osteomalacia or rickets) and those in which the osteoblasts are primarily deficient in laying down osteoid tissue; this is osteoporosis.

18. Albright, Fuller; Bloomberg, Esther, and Parsons, W.: The Effect of Estradiol Benzoate and Testosterone Propionate on the Disordered Calcium, Phosphorus and Nitrogen Metabolisms in Two Cases of Cushing's Syndrome Without Adrenal Tumors, read before the Twenty-Fourth Annual Scientific Session of the Association for the Study of Internal Secretions, New York, June 11, 1940.

19. Crooke, A. C., and Callow, R. K.: The Differential Diagnosis of Forms of Basophilism (Cushing's Syndrome) Particularly by the Estimation of Urinary Androgens, Quart. J. Med. **8**: 233, 1939. Fraser, Forbes, Albright, Sulkowitch and Reifenstein.[21]

20. Gardner, W. U., and Pfeiffer, C. A.: Inhibition of Estrogenic Effects on Skeleton by Testosterone Injections, Proc. Soc. Exper. Biol. & Med. **38**: 599, 1938.

21. Fraser, R.; Forbes, A. P.; Albright, Fuller; Sulkowitch, H. W., and Reifenstein, E. C., Jr.: Colorimetric Estimation of "Seventeen Ketosteroids" in Urine; A Survey of the Use of This Test in Endocrine Investigation, Diagnosis and Therapy, J. Clin. Endocrinol., to be published.

22. Albright, Fuller; Sulkowitch, H. W., and Bloomberg, Esther: Further Experience in the Diagnosis of Hyperparathyroidism, Including a Discussion of Cases with a Minimal Degree of Hyperparathyroidism, Am. J. M. Sc. **193**: 800, 1937.

2. Emphasis is placed on the fact that osteoporosis is not a disorder of calcium metabolism but rather an atrophy of the bone matrix.

3. Factors in the causation of osteoporosis are disuse and senescence; that faulty diet is a factor, in our opinion, has not been established.

4. Because of the constant tendency of osteoporosis to occur in women after the menopause and the beneficial effect of estrogen therapy on the retention of calcium in this condition, we believe that the postmenopausal state is the most common etiologic factor.

5. Of 42 patients under the age of 65 with generalized osteoporosis, 40 were women who had gone through the menopause (physiologic 30 cases, artificial 10 cases); only 2 were men; there were no cases in women before the menopause.

6. Three of the 42 patients had had thyrotoxicosis; whether this had been a factor in the causation of the disease it is impossible to state.

7. Postmenopausal osteoporosis has a predilection to involve the spine and the pelvis; the long bones are less likely to be involved; the skull, in contrast to osteitis fibrosa generalisata, is almost never involved.

8. There is considerable evidence that patients with postmenopausal osteoporosis have a tendency to atrophy of other tissues, notably the skin.

9. In 2 cases postmenopausal osteoporosis was complicated by superimposed Paget's disease; the modification of the latter disease by the former is noteworthy.

10. One case of postmenopausal osteoporosis was complicated by superimposed hyperparathyroidism; the latter disease was modified by the former.

TREATMENT OF DEMENTIA PARALYTICA

A FIVE YEAR COMPARATIVE STUDY OF ARTIFICIAL FEVER THERAPY AND THERAPEUTIC MALARIA IN TWO HUNDRED AND THIRTY-TWO CASES

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This is a report of a five year study comparing the therapeutic efficiency of artificial fever therapy and of therapeutic malaria. The preliminary report of this study was made in 1936.[1] There is nothing unique in the use of either malarial therapy or artificial fever, the former having been advocated by Wagner von Jauregg's original report in 1917 and the latter by Neymann and Osborne[2] in 1929. For reasons not entirely clear to us certain clinics treating patients with neurosyphilis have been skeptical of the therapeutic value of artificial fever in this neuropsychiatric disorder. Because of this apparent prejudice against a new method we felt it wise to observe a series of patients, taking alternate patients in the series for treatment with each method. Patients were assigned to the artificial fever or malaria series in alternation as they were admitted to the Colorado Psychopathic Hospital and Clinic, that is, patient 1 went to the malaria series, patient 2 to the artificial fever series and so on. The postfever care has been according to the same plan in all cases from both series and has consisted of intensive chemotherapy with tryparsamide, neoarsphenamine and bismuth compounds according to the plan given in the accompanying outline.

Since the inauguration of this study there have been numerous reports[3] advocating the use of artificial fever therapy in the treatment of neurosyphilis and others reporting on the present status of therapeutic malaria.[4] The best statistical analysis of a comparison of the therapeutic efficiency of the two methods used independently has been made by the Cooperative Clinic Group.[5] The historical background of this study was traced in the preliminary report and will not be repeated here.

METHOD

All patients treated by both methods were subjected to detailed clinical and laboratory studies before treatment was instituted. All were studied by one of us. The treatment of all patients in both the malaria and the artificial fever series was administered in this clinic under our direct observation and supervision. Follow-up studies were made at six month intervals in the outpatient department of the Colorado Psychopathic Hospital except when the patients were incarcerated in the Colorado State Hospital. In such cases the follow-up studies were made by a physician from the Colorado Psychopathic Hospital. The majority of the postfever chemotherapy was administered in the outpatient department of the Colorado Psychopathic Hospital, although a few patients received their treatment from private physicians according to our therapeutic plan. Because of the cooperation of these private physicians and the staff of the Colorado State Hospital there is little difference in the type of follow-up care of these patients treated outside the Colorado Psychopathic Hospital Clinic. Social data, appointments for follow-up examinations and general aid in keeping track of the patients were handled efficiently by a trained psychiatric social worker who has this study as her principal duty. All follow-up examinations were made by a trained psychiatrist on duty in this hospital or in the Colorado State Hospital. The physicians making these follow-up studies were not aware of which type of fever therapy the patient had originally received. The patients in the malaria series in most instances received fifty hours of fever at 104 F. or more, although at times the patient's condition would not allow this amount of fever to be given. In the first three years of the study patients in the artificial fever series received fifty hours of fever at rectal temperatures of 105 F. to 106 F., given as ten treatments of five hours each. During the last two years of the study the artificial fever group received only thirty-six hours of fever but at a rectal tempera-

From the Colorado Psychopathic Hospital, University of Colorado School of Medicine.

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4. Hutchings, C. W.: The Results of Ten Years of Malarial Therapy, Psychiat. Quart. **10**: 99-109 (Jan.) 1936. O'Leary, P. A.: Nonspecific Treatment of Syphilis, J. A. M. A. **110**: 42-45 (Jan. 1) 1938. Branche, G. C.: Therapeutic Quartan Malaria in the Treatment of Neurosyphilis Among Negroes, Am. J. Psychiat. **96**: 967-978 (Jan.) 1940.

5. O'Leary, P. A.; Brantsch, W. L.; Ebaugh, F. G.; Simpson, W. M.; Solomon, H. C.; Warren, S. L.; Vonderlehr, R. A.; Usilton, Lida J., and Sollins, I. V.: Malaria and Artificial Fever in the Treatment of Paresis, J. A. M. A. **115**: 677-681 (Aug. 31) 1940.

ture of 105.8 F. given as twelve treatments of three hours each. We could notice no difference in the results obtained from the shorter, more frequent treatments, and it enabled us to treat a greater number of patients in the artificial fever department. After fever therapy by either method complete laboratory and clinical studies were again made. Patients responding favorably were

Outline of Treatment of Dementia Paralytica at the Colorado Psychopathic Hospital

Therapeutic Malaria
Fifty hours at 104 F.
Eight to ten chills
No chemotherapy possible

or

Artificial Fever Therapy
Thirty-six hours at 105.8 F.
Twelve three hour treatments
Simultaneous chemotherapy

Follow-Up Treatment

A. First year:
(a) Six months of tryparsamide, 3 Gm. weekly
(b) Physical, mental, neurologic and complete serologic check-up
(c) Four months of bismuth salicylate, 0.26 Gm. weekly
(d) Two months of neoarsphenamine, 0.6 Gm. weekly
(e) Repeat examinations outlined under (b)

B. Second year:
Repeat procedure outlined for first year

C. Third year:
Repeat procedure outlined for first year

All treatment is continuous. Eyegrounds and visual fields must be checked frequently. Repeat series as often as necessary. Patients not improved after three years will probably not benefit from further treatment.

transferred to the outpatient department and reported weekly for follow-up treatment. A small percentage returned to their private physicians for follow-up care, but they were encouraged to return to the clinic each six months for reexamination. The social worker keeps a rotating roster, and each six months each patient's name appears automatically. She then makes contact with the patient and arranges for a reexamination in the clinic. Those patients transferred to the state hospital in Pueblo are checked in that institution. We have had the usual difficulty in following our patients in their travels about the country, but the assignment of a social service worker to the task of getting the patients in for examination has made our follow-up treatments and examinations more complete than was possible prior to the inauguration of this system. For example, we were able to follow all of our patients treated with malaria and reported in the preliminary study [1] and 66 per cent of the artificial fever series studied in the same group for the entire five years or until they died. The periodic reexaminations consist of complete physical, neurologic and mental check-ups and serologic examinations of the blood and spinal fluid. It is interesting to note that most of the patients lost sight of during the follow-up period were patients who responded favorably to treatment and after two or three years of follow-up care felt free of symptoms and refused to come back for further examination. Some of those lost sight of moved out of the state and could not be reached. Most of the patients doing poorly have been admitted to the state hospital or have continued to come to this clinic seeking aid for their trouble. The deaths are, as far as we know, all recorded in the data.

RESULTS

The statistical evaluation of the results of any clinical research study is difficult at best. In a disease such as neurosyphilis there are so many variables, such as the duration of the infection before treatment, the type and quantity of prefever chemotherapy, the age and the physical and social status of the patient, that any statistical presentation is open to criticism. A detailed statistical analysis of a large group of cases was made by the Cooperative Clinical Group.[5] We supplied a number of the cases in that study, and both the fever and the malaria series of the first year were included in that survey. We do not feel competent to make a detailed statistical breakdown of our data. We wish to present our general results and to mention certain trends noted in individual cases.

That the series are fairly comparable is indicated by the fact that 32 per cent of the patients in the artificial fever series and 31 per cent of those in the therapeutic malaria series were persons with advanced or so-called group A dementia paralytica. The average age of the artificial fever group was 40 years, and the average of the malaria group was 42.6 years, and the duration of symptoms prior to treatment was twenty-two and four-fifths months in the fever group and seventeen and one-fifth months in the malaria group. The data concerning prefever chemotherapy included vague recollections of "shots" taken years before the development of dementia paralytica as well as accurate clinical records from other hospitals and clinics. The reliability of the data varied so greatly in both series that no attempt was made at any evaluation of the influence it may have had on the course of the disease.

It will be noted in table 1 that more patients were treated by artificial fever than by therapeutic malaria. This was not due to variation in the selection of cases, but we have included in the artificial fever group 37 patients rejected from the comparative study because of the presence of diabetes, healed tuberculosis, cerebral arteriosclerosis, chronic nephritis and mild cardiac decompensation. Patients suffering from these disorders are not suitable for malaria therapy but may be given artificial fever with caution. In some instances the rectal temperature of the artificial fever was lowered to 104 F. It was felt, however, after a study of these cases that they should be lumped with the other cases suitable for either form of treatment in that these disorders probably do not greatly influence the course of the neurosyphilis other than by contraindicating malaria therapy. The results in this small group did not significantly alter the general picture.

TABLE 1.—*Types of Treatment and Clinical Results*

Clinical Status	Artificial Fever		Therapeutic Malaria	
	No. of Cases	Percentage	No. of Cases	Percentage
Remission	25	19	7	7
Improved	68	50 (69)	50	51 (58)
Unimproved	31	22	27	27
Died within three months of treatment	2	1.4	5	5
Died subsequently	8	6.6	9	9
Total	134	99	98	99

The general results of the study are included in table 1. Remission or improvement was noted in 69 per cent of the artificial fever group as compared with 58 per cent in the therapeutic malaria group. By remission is meant the condition of patients who are showing no clinical symptoms of their disorder and who have been able to resume their previous role in the community. Improved patients are those who are definitely better than when treatment was instituted but are operating at a lowered level of efficiency. The inter-

esting fact is that there was approximately the same difference between the two series in the preliminary or first year of this study. In other words, the rate of improvement during follow-up care and the rate of relapse are approximately the same in the two series, and the difference in our hands seems to be a difference in immediate results.

TABLE 2.—*Group Classification in Relation to Clinical Results*

	Artificial Fever						Therapeutic Malaria					
	Group A		Group B		Group C		Group A		Group B		Group C	
Clinical Status	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Remission	0	0	16	23	9	45	0	0	4	7	3	25
Improved	18	41	39	54	11	55	9	29	35	64	6	50
Unimproved	19	43	12	17	0	0	15	48	11	20	1	8
Died	7	16	3	4	0	0	7	23	5	9	2	17
Total	44	100	70	98	20	100	31	100	55	100	12	100

We cannot be certain as to the reasons for this difference, but some of the factors which may play a role will be mentioned. The most important difference in the two series may be the fact that with artificial fever therapy the patients may be safely treated at higher levels of temperature than is possible with therapeutic malaria. The importance of high levels of temperature has been shown by the Cooperative Clinical Group study.[5] Another factor which may play a role is that patients usually gain weight during artificial fever therapy and in most instances are in better physical condition at the conclusion of the febrile period than when it was first instituted. The patients with malaria, on the other hand, usually lose weight and have some degree of anemia in spite of energetic attempts to prevent it. We originally felt that the difference was largely due to the fact that we administered tryparsamide with each artificial fever treatment. In order to check on this for the last two years of this study we did not give tryparsamide during the period of fever. In place of this, half of the patients with artificial fever received 0.3 Gm. of neoarsphenamine and 0.26 Gm. of bismuth salicylate during every other heating and the other half of the patients treated with artificial fever during the same period received no chemotherapy. We could see no significant difference between the two groups, nor could we see any significant difference between them and the larger group receiving tryparsamide with their heating. Therefore we believe that the first two factors are the important ones, although the added chemotherapy must be of some benefit even though it failed to be statistically significant in this relatively small series.

Table 2 presents the clinical results according to the severity of the infection. Group A is advanced or severe dementia paralytica, group B the intermediate and group C the mild form. Detailed definitions of this grouping are contained in the original article.[1] The results are good with both methods in the mild cases and treatment becomes progressively less effective as the severity of the process increases. We obtained no true remissions in the advanced or A group by any form of treatment, but in many instances we were able to bring about definite improvements by either method of nonspecific treatment. The report of the Cooperative Clinical Group [5] showed artificial fever to be ten times as effective as therapeutic malaria in advanced dementia paralytica. Our study also shows a superiority of the artificial fever method in this group (table 2) but a superiority of only 12 per cent.

Our experience parallels that of Solomon [6] and others that intensive follow-up chemotherapy is essential if optimum sustained results are to be obtained. The variation in results reported from various clinics might be explained on the basis of care in follow-up treatment and examinations. The fact that the results in our series are superior to those reported in some clinics and inferior to others may well be due to this fact. We have found that in recent years the employment of a social worker and a greater drive to keep patients coming in for treatment and check-ups have certainly increased the beneficial results obtained in the patients given malaria therapy as compared to those patients treated with malaria before this study was inaugurated. For example, in the years 1925 to 1931 we treated 219 patients with dementia paralytica with therapeutic malaria. Of this group 45.6 per cent showed a remission or improvement. Our present malaria series reveals that 58 per cent of the patients are in some manner improved by the treatment, which means an improvement of 12.4 per cent in results from therapeutic malaria in the present study. We believe that this difference is due largely to greater care during the course of the malaria and greater emphasis on follow-up chemotherapy and supervision. Both of these groups were treated with therapeutic malaria in this hospital and, incidentally, with the same strain of tertian malaria.

The serologic response appears to show a greater modification in the group treated with artificial fever (table 3). The difference in results is not great and roughly parallels the difference in the rate of clinical remission. While we noted no direct correlation between alteration in serologic conditions and clinical remission in individual cases, we do find a higher percentage of serologic reversals in the group in both series showing great improvement than in those showing less improvement or no change in clinical status. Reversal or even great alterations in the serologic state immediately after the course of fever or malaria were rare but when they did occur seemed to indicate a good clinical prognosis. In several cases, on the other hand, great clinical improvement has been maintained in persons with spinal fluid persistently positive for syphilis. In our small series a decrease in the cell count and protein of the spinal fluid to within normal limits immediately

TABLE 3.—*Serologic Results in Cerebrospinal Fluid*

	Artificial Fever		Therapeutic Malaria	
Clinical Status	Number of Cases	Percentage	Number of Cases	Percentage
Reversed	15	11	6	6.1
Improved	47	35	28	28.5
Unmodified	47	35	40	40.8
Unable to check	25	18	24	24.4
Total	134	99	98	99.8

after treatment with artificial or malarial fever usually indicated that a considerable alteration or reversal of the Wassermann reaction and the colloidal gold curve was to be expected in six to twelve months provided the patient continued on the program of postfever chemotherapy. The changes in the status of the blood serum are inconstant and of practically no value in evaluating either the clinical course or the status of the spinal fluid.

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CONCLUSIONS

In a five year study 232 patients with dementia paralytica have been treated with either therapeutic malaria or artificial fever therapy. The follow-up therapy in the two groups has been as nearly identical as the vagaries of clinical practice will allow. The method of therapy with artificial fever has been safer and has been productive of better results. The importance of follow-up care is emphasized. Improvement in the care of patients during malaria therapy and more attention to follow-up medication has improved the results of malaria therapy in our clinic, although these results still remain inferior to the results obtained with artificial fever therapy.

Patients with physical contraindications to therapeutic malaria may, in many instances, be safely treated with artificial fever therapy. Either method is reasonably efficient if properly managed and if general follow-up treatment and care are adequate.

The serologic responses roughly parallel the clinical results in the two series. Careful, periodic, clinical reexamination offers the best guide for therapy and gives the most reliable data for evaluation of results.

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CALCIUM DEPOSITS IN THE SHOULDER AND SUBACROMIAL BURSITIS

A SURVEY OF 12,122 SHOULDERS

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The title of this paper is purposely indefinite. It is intended to cover calcium deposits observed in the tendons of the four short rotator muscles of the shoulder and the inflammatory condition of the overlying serous bursa to which these deposits not infrequently give rise. That others have experienced difficulty in devising an appropriate label for this pathologic entity is well attested by the diversity of captions used by many who have written on the subject in the last two or three decades. It has been described as "periarticular calcifications," [1] "para-articular calcifications," [2] "subacromial" or "subdeltoid calcifications," [3] "humeroscapular" or "scapulohumeral periarthritis," [4] "para-arthritis," [5] "Duplay's disease," [6] "calcified bursitis," [7] "calcic bursitis," [8] "calcification of the subacromial bursa," [9] "rheumatism" or "neuritis" [10] and "painful shoulder." [11]

The fact remains that calcium deposits in the tendinous cuff which forms the capsule of the shoulder joint have for some time been recognized as a potential source of shoulder pain. The anatomy of this region, the pathologic changes encountered, the composition of the calcium deposits and their relation to the subacromial bursa are now quite well known, chiefly as the result of Codman's work on the shoulder; [12] yet little precise information is available as to the incidence of such deposits in the general population, what factors cause or contribute to their formation and what plan of treatment offers the best prospects of relief and cure of those deposits which give rise to symptoms.

Through observation of a large group of presumably normal persons over a period of years, much interesting and pertinent material on these points has been accumulated.

During the three year period from 1937 through 1939, 6,061 unselected persons were subjected to physical and fluoroscopic examination of both shoulders in connection with a routine examination at the home office of the Metropolitan Life Insurance Company; 5,061 were company employees while 1,000 were applicants for insurance or for employment. Of the whole group 165 (2.7 per cent) were found to have calcium in sufficient amount to show on fluoroscopy in one or both shoulders. The incidence of calcium formation was exactly the same in the employee and the nonemployee groups.

An analysis of both groups on the basis of sex, age and occupation has been made. Since, however, it has been possible to study the 5,061 employees much more intensively and to follow them with reexamination at annual intervals, the remainder of this report will be confined to them unless expressly stated otherwise.

Before employment each applicant is subjected to a thorough physical and laboratory examination, including roentgenograms of the chest. Throughout the period of employment a detailed medical record is kept of serious and minor ailments as well as of annual physical and fluoroscopic examinations of the heart and lungs.

The 5,061 employees were taken in succession as they came for the annual health examination. They include 3,883 females and 1,178 males, of whom 89.4 per cent were under the age of 40. Seventy and nine-tenths per cent did purely or mostly clerical work, 23.2 per cent used either a typewriter or similar manually operated machine exclusively, while the remainder were employed in miscellaneous occupations such as messengers, elevator operators, porters and cleaners.

It is obvious that the group studied constitutes a selected portion of the general population as to physical condition (preemployment and annual examinations), sex (76.7 per cent females), age (89.4 per cent under 40) and occupation (94.1 per cent clerks or typists).

Dr. H. H. Fellows, assistant medical director of the Metropolitan Life Insurance Company, and Drs. R. K. Felter, J. H. Inkster, Eleanor Murphy, Mary E. O'Sullivan and Peter Sabatelle assisted in this study.

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It is in the main a cross section of the so-called white collar class of workers.

In the course of routine annual fluoroscopic examination of 5,061 employees, visible calcium deposits were found in one or both shoulders of 138 (2.7 per cent).

TECHNIC OF EXAMINATION

Since this investigation was based on a search of several thousand supposedly normal shoulders for possible calcium deposits, it is apparent that roentgenography of each shoulder was not only highly unpractical but essentially valueless. Not only would many films have to be taken of each shoulder in different planes but this would have to be repeated each time the person was subsequently examined, and even then some calcium collections would be overlooked.

Good sized deposits may easily be missed unless they are seen in profile. It is quite usual for the calcium to be spread out in a thin layer, which is effectively obscured by the humeral head until the arm is rotated so that the roentgen rays have to traverse not the thickness but the width or length of the deposit (fig. 1). For these reasons fluoroscopy is preferable to roentgenography in detecting the presence of calcium deposits and should never be omitted as a preliminary procedure. Similarly, no deposit should be considered completely absorbed unless the shoulder has been checked by fluoroscopy (fig. 3). Both shoulders should be examined in every case.

My practice has been to examine the shoulder with the fluoroscope throughout its full range of motion and take a spot-film of each deposit as it appears in profile, using a specially devised casette holder which is hung on the fluoroscopic screen. The details of shoulder examination by a combination of fluoroscopy and spot-film roentgenography are beyond the scope of this paper and will be discussed elsewhere.[12a] Excellent technical descriptions of roentgenography of the shoulder are available in the recent literature.[13]

ETIOLOGIC FACTORS

Care must be exercised in drawing conclusions as to the effect of sex, age, occupation and other factors on the formation of calcium deposits. Only percentages based on an adequate number of persons examined in each group are of significance in a comparative study.

Sex.—Although the majority of persons with calcium deposit were females, deposits were found with greater relative frequency in males (3.6 per cent) than females (2.5 per cent) in the whole employee group.

Age.—Again, despite the fact that 70.3 per cent of all positive results were found in persons under 40, the incidence of calcium deposits in both males and females rose with the advance of years, by decades, up to the age of 50, after which it declined sharply.

Blood Calcium.—Blood calcium values were determined for 20 persons of this series, all with large deposits in one or both shoulders. Some were suffering from an acute bursitis; others were not. In every instance normal values were obtained.

Infection.—No one has succeeded in linking calcium deposition in these tendons or the associated bursitis to a local infectious process (cultures taken at operation have always been negative; operative wounds do not suppurate) or to a past or present systemic infection. The opinion has been expressed that infection plays no part in the formation of calcium;[14] the present investigation confirms this theory.

A careful search of the detailed medical records of all 138 persons showing calcium deposits was made for serious illness, arthritis, rheumatism and foci of infection, but none of these factors appeared to influence the formation or course of these deposits in the slightest degree. One hundred and seven (72 per cent) of the 138 employees with deposits were in the company's employ and subject to close, continuous medical observation for a period of ten years or longer, many of them for more than thirty years; yet of these only 23 had suffered any serious illness, and only 9 had a record of arthritis or rheumatism in any form. Fifty had some focus or foci of infection serious enough to require medical attention, usually of minor degree, at some time during their employment; more than half were tonsils and most of the remainder were sinuses.

Occupation.—Since there were very few male typists in this series of cases, a study of the effect of occupation on calcium deposit formation must be confined to females. A glance at the table will show that women typists had a significantly higher incidence of deposits than women clerks throughout all age groups up to the

Calcium Deposits in the Shoulder: A Survey of 5,061 Home Office Employees of the Metropolitan Life Insurance Company Grouped According to Sex, Age and Occupation

Age at Examination	Males												Females											
	Total			Clerks			Typists			Miscellaneous			Total			Clerks			Typists			Miscellaneous		
		With Deposits			With Deposits			With Deposits			With Deposits			With Deposits			With Deposits			With Deposits			With Deposits	
	Number Examined	Number	Per Cent	Number Examined	Number	Per Cent	Number Examined	Number	Per Cent	Number Examined	Number	Per Cent	Number Examined	Number	Per Cent	Number Examined	Number	Per Cent	Number Examined	Number	Per Cent	Number Examined	Number	Per Cent
Total	1,178	42	3.6	954	34	3.6	14	1	7.0	210	7	3.3	3,883	96	2.5	2,636	50	1.9	1,161	42	3.6	86	4	4.6
17-19	4	..	...	...	...	...	..	..	...	4	..	...	115	..	...	81	..	...	34	..	...	..	..	...
20-29	533	7	1.3	471	5	1.1	12	1	8.3	50	1	2.0	2,679	40	1.5	1,721	14	0.8	932	25	2.7	26	1	3.8
30-39	403	10	2.5	354	10	2.8	2	..	...	47	..	...	704	40	5.0	407	24	4.9	167	15	9.0	20	1	5.0
40-49	138	16	11.6	82	13	15.9	..	..	...	56	3	5.4	186	13	7.0	127	9	6.6	22	2	9.1	27	2	7.4
50-59	73	5	6.8	33	3	9.1	..	..	...	40	2	5.0	93	3	3.2	79	3	3.8	2	..	...	12	..	...
60-70	27	4	14.8	14	3	21.4	..	..	...	13	1	7.7	16	..	...	11	..	...	4	..	...	1	..	...

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V 19

age of 50. This seems to provide a positive answer to the question raised by Codman [12] as to the effect of occupation on the formation of deposits, and it substantiates his impression that "Millions of years of heredity have not prepared the modern stenographer or machine operator to keep their supraspinatus tendons stretched and under tension, on the qui vive hour after hour, day after day."

Therefore, while it cannot be proved that any particular job was responsible for a certain calcium deposit, nevertheless occupation as a causative factor must be given due consideration in deciding whether the work in question produced or helped to produce the deposit, when that work involves constant abduction of the arms for months and years.

Trauma.—The relation, if any, of trauma to calcium deposits and acute bursitis is one of the most interesting and at the same time most difficult problems presented by this symptom complex. "As these little calcified deposits now cause loss to the insurance companies, they are assuming more importance than when they only bothered the individual patient." [12] Any claim for compensation in this connection immediately raises the questions: Did the alleged trauma produce the lesion or aggravate an existing lesion, or was it merely coincidental?

Of 41 [15] shoulders with an acute attack of bursitis in only 7 was there a clearcut history of antecedent trauma which could reasonably be considered as precipitating the acute attack, and most of these traumas were of trivial nature. They are so typical as to be worthy of verbatim report: "while moving bureau to attic," "slipped on stairs and fell," "while gardening on return from vacation," "while scrubbing floor," "while reaching up to fix windshield wiper," "after a fall," "while putting on my coat."

In the remaining 34 acute attacks of bursitis the patient was unaware of any specific trauma or exertion as responsible for the condition. Several patients were

Fig. 1.—A. W., a woman aged 31, a typist, had multiple calcium deposits detected by fluoroscopy and roentgenographed by spot-film technic. Illustrates the importance of fluoroscopic examination, with arm rotation, to bring out deposits hidden by the humeral head. She had had slight symptoms in both shoulders for four years, diagnosed "myositis" (no roentgenograms). *A, B, C:* Right shoulder: external, mid and internal rotation. *D, E, F:* Left shoulder: external, mid and internal rotation.

merely awakened suddenly during the night, without warning, by acute pain in the shoulder. It should be noted, furthermore, that many of these patients had had known calcium deposits in one or both shoulders with little or no symptoms for months or years prior to the acute attack.

In this series of cases, therefore, there is no statistical evidence that any single trauma per se was responsible for calcium deposition or for the acute attack of bursitis associated therewith. Trauma, when it did occur, has

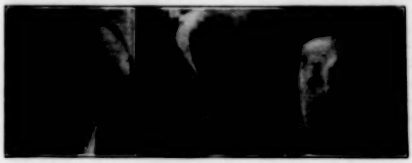

Fig. 2.—M. F., a man aged 57, a clerk, had distention of bursa, greatly increased by treatment with heat. He had had slight symptoms diagnosed "myositis" (no roentgenograms were made) for three years, unrelieved by baking. There was sudden onset of acute bursitis (*A*). Symptoms were aggravated by three weeks of baking (*B*). Ultimate complete relief occurred with disappearance of calcium in one year (*C*).

seemed to be coincidental [16] or at most the straw that broke the camel's back by merely precipitating an inevitable bursitis.

LOCATION AND SIZE OF DEPOSITS

Forty-six and four-tenths per cent of the 138 patients with calcium had bilateral deposits, calcium being visible in a total of 202 shoulders. Among those with unilateral deposits, the right shoulder was involved twice as often as the left.

As the tendons of the short rotators, the supraspinatus, infraspinatus, teres minor and subscapularis, are indistinguishably fused to form the capsule of the shoulder joint, it is at first difficult to determine which tendon contains the deposit. Practically, it makes little difference; the important thing is to locate the deposit in profile and note the rotation of the arm which brings it there. With practice and the use of a suitable spot-film roentgen technic, it is possible to attain a fairly high degree of accuracy in this procedure.[12a]

Fifty-one and five-tenths per cent of the involved shoulders had calcium in the supraspinatus portion of the cuff, 44.5 per cent in the infraspinatus and 23.3 per cent in the teres minor. Only 5 shoulders showed calcium in the subscapularis. Calcium was visible in the subacromial bursa in 25 shoulders (figs. 2 and 3). This may seem surprising in view of the fact that there were 41 shoulders with an acute attack of bursitis, yet it confirms a rather common operative finding of milky, calcium-containing fluid in a bursa in an acute state which did not show on roentgen examination.

Variations in roentgen technic, in the contour of the person examined and in the shape of the deposit make classification of calcium formations according to size extremely difficult, yet a grouping of deposits from this standpoint is of considerable value in treatment and prognosis. For the purpose of this report, the following basis of comparison was used:

Large: Deposits 1.5 cm. or longer in their greatest profile dimension.
Medium: All others except:
Tiny: Those barely perceptible on fluoroscopic examination.

According to this classification, 16.3 per cent of the shoulders showing deposits contained one or more large deposits, 54.5 per cent had medium ones and 50 per

15. Eighteen of these occurred among the 138 employees in whom deposits were found on routine fluoroscopy; 23 occurred among 29 additional employees who were seen initially for relief of their symptoms.

16. Carnett, J. B., and Case, E. A.: Clinical and Pathological Discussion of So-Called Subacromial Bursitis, S. Clin. North America **9**: 1107-1126 (Oct.) 1929. Codman.[12]

cent had tiny accumulations. Multiple deposits occurred in 20.3 per cent of the involved shoulders. In a number of cases the joint capsule was studded with bits of calcium as though with buckshot (fig. 1).

APPEARANCE AND DISAPPEARANCE OF CALCIUM

The slowly progressive accumulation of calcium and its regression are clearly depicted in a series of roentgenograms taken of one patient during the past eight years. A woman aged 29, a machine operator, had had painful deposits in both shoulders since 1932 (fig. 3). An acute attack of bursitis of the right shoulder in 1934 was partially relieved by baking and diathermy, with regression but not complete disappearance of the deposit. Meanwhile the calcium collection in the left shoulder has grown steadily larger, with progressively increasing symptoms. She manages to perform her work and thus far has consistently refused treatment of the left shoulder, although she has repeatedly been advised to have the calcium removed. In view of the past history of this shoulder it will be of particular interest to observe whether the onset of the acute attack of bursitis, which I believe is inevitable, coincides with any trauma.

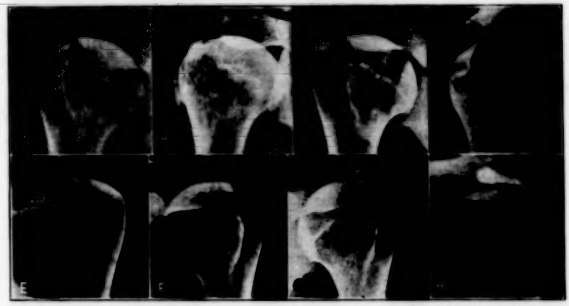

Fig. 3.—F. D., a woman aged 29, a machine operator, had calcium deposits with symptoms in both shoulders for eight years (referred to in text). *Right Shoulder: A* (1932), two medium size deposits; *B* (1934), acute bursitis; *C* (1938), calcium apparently all gone (roentgenograms without fluoroscopic examination); *D* (1939), calcium residue persists (fluoroscopic examination, with rotation, and spot-film roentgenograms). *Left Shoulder:* Progressive increase in deposit and symptoms: *E*, 1932; *F*, 1935; *G*, 1938; *H*, 1939.

Calcium appeared subsequent to a negative fluoroscopic examination in 29 (14.4 per cent) of the 202 shoulders showing deposits. All these deposits were seen within one year of the first (negative) fluoroscopic examination, 3 of them being discovered within as short a period as two months. It is conceivable that 1 or 2 of these may have been overlooked at the first examination, before our fluoroscopy technic had been fully developed; certainly the majority were not. Two were large deposits and half the rest were of medium size, easily seen.

Though calcium has often been observed to regress under treatment, and for that matter without treatment, in only 13 shoulders did it entirely disappear within the period of this study. Nine of the 13 presented symptoms. Of these, in 2 there was no treatment of any kind given, in 2 others the deposit was removed by operation and in 5 the deposit disappeared coincidentally with baking or diathermy. In the remaining 4 shoulders in which the calcium disappeared under observation there were never any symptoms nor was any treatment given; all these deposits were medium sized or tiny. Every large deposit gave rise to symptoms before disappearing completely.

SYMPTOMS

Seventy (34.6 per cent) of the 202 involved shoulders caused some degree of pain or discomfort at one time or another, either prior to or during the period of observation. This varied from an occasional "twinge" or "hitch" in dressing or in doing the hair to complete disability, with intense pain and muscular spasm. Nocturnal discomfort was most frequently mentioned, consisting of great difficulty in finding a comfortable position in bed at night. Probably this is due in some measure to release of traction which the weight of the arm maintains with the patient upright during the day; with the traction removed, muscle tonus and spasm cause increased pressure on the painful deposit. In addition, of course, it is hard to sleep on one side all night, and there is nothing to divert the patient's attention from the affliction.

The majority of persons affected, on adequate questioning, were able to recall having had "trouble" with the shoulder previously. However, it is surprising how often even severe pain may be forgotten, for complaints were found in the past medical records of 5 persons who stated that they had never suffered.

Twenty-two (10.9 per cent) of the 202 involved shoulders gave rise to symptoms for the first time subsequent to discovery of the calcium on fluoroscopic examination; in 7 of these calcium deposits were observed to have remained without symptoms for from one to two years.

In 5 shoulders symptoms which called attention to visible deposits first developed subsequent to a negative fluoroscopic examination; 2 at two months, 1 at four months, 1 at six months and 1 at about one year after the negative examination.

In order to estimate the severity of symptoms, the 70 painful shoulders have been divided into three groups: acute, mild and slight. Symptoms are notoriously difficult to evaluate. Some persons bear pain well and others do not. However, there is no mistaking an acute attack of bursitis; these are the really "acute." Other shoulders with less pain but sufficient to require treatment are classed as "mild" and those which cause some annoyance but no real pain form the "slight" group.

On this basis, the symptoms in 18 shoulders were acute, in 22 mild and in 30 slight. The size of the deposit in general accorded with the symptoms complained of, yet it is interesting to note that one third of the large deposits gave rise to no complaints whatever while under observation (fig. 4).

TREATMENT

The question of what form of treatment offers the best prospects of relief or cure of painful shoulder deposits is a difficult one. This affliction is sometimes self limited and self curative. It is common knowledge that an occasional case may become temporarily improved or even to all intents and purposes cured without treatment. I have seen this happen in 4 shoulders which went untreated and had complete

spontaneous remission of symptoms. This fact, of course, makes it possible for the proponent of any particular form of treatment to claim cures for his own method. Thus an element of confusion and uncertainty is added to the problem, and one is wise to keep this in mind when analyzing any series of end results.

The present report is no exception. It is admitted that a certain (unknown) number of those patients listed as cured by any one of the modes of treatment which were used might have obtained full relief without treatment. However, as this factor of uncertainty applies equally to all the therapeutic methods under consideration, a comparison of the end results of those methods is still significant.

During the three year period of investigation there were seen 40 shoulders of patients not included in this study in which relief from painful deposits was sought. In estimating results of treatment, these 40 shoulders have been added to the 70 painful shoulders in which the deposits were first found on routine fluoroscopic examination, making a total of 110 painful shoulders which came under observation. Among these 110 shoulders were 33 in which treatment was refused. The other 77 received baking, diathermy, excision or irrigation of deposits, singly or in combination, with ultimate complete relief in half and partial amelioration of symptoms in most of the rest.

A mere statistical summary such as this does not, however, tell the whole story. Many of those patients counted as fully relieved by baking or diathermy or both were under treatment, with pain and disability, off and on for years. As many as sixty to eighty diathermy treatments were given to a single shoulder over a period of six to eight months in at least 2 instances, with little or no relief. Apart from the physical suffering incurred, the expense of treatment and the number of work days lost are factors of considerable importance to these patients and to insurance companies, when the latter are involved.

Frequently an acute attack was precipitated or a somewhat painful shoulder made worse by the application of heat (fig. 2). On the other hand there are occasional patients who have been completely relieved by a few baking or diathermy treatments; these I believe are ones which would have had spontaneous remission of symptoms regardless of treatment. In most cases there has been temporary or partial relief following conservative measures, with subsequent recurrent attacks in the same shoulder.

Although no conclusion as to the relative merits of these different modes of treatment can as yet be supported by statistics, owing to the small number of treated shoulders available, I have acquired certain convictions regarding treatment as a result both of this study and of experience in practice.

I agree with those [17] who feel that the best treatment for the acute attack is prompt excision of the deposit. In experienced hands it is a relatively minor procedure, done under local or general anesthesia through a small incision. It gives immediate, certain and complete relief which so far as I know has been permanent. The patients have had an average hospital stay of four days and have been able to resume their usual duties, with unrestricted shoulder motion, in three weeks.

I recognize the fact that irrigation [18] will give relief in selected cases of acute involvement in which the bursa is well distended and free of adhesions, but it too is an operative procedure (less certain than excision of the deposit), to be done under anesthesia in a hospital, and I am not convinced that all the calcium, from tendon as well as from bursa, can be removed in this way in every case.

The application of heat by one modality or another [19] is therapeutically sound, but as an adjuvant rather than as a primary or basic form of treatment. I use it following operation to speed healing and recovery.

Not one of the painful shoulders in this series was subjected to roentgen therapy.[20]

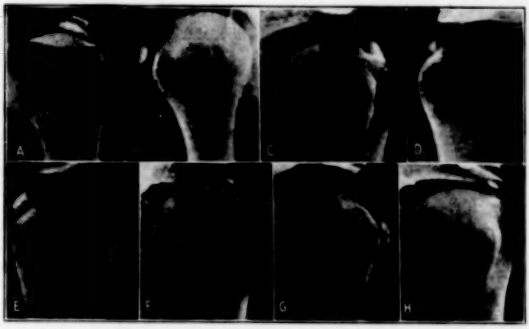

Fig. 4.—Some large calcium deposits, thus far without symptoms, found on routine fluoroscopic examination: *A*, R. M., ♀, 35, typist. *B*, V. S., ♀, cleaner. *C*, K. D., ♀, 45, clerk. *D*, I. R., ♀, 46, clerk. *E*, P. T., ♂, machine operator. *F*, E. B., ♀, 42 clerk. *G*, H. T., ♀, typist. *H*, R. K., ♂, 40, clerk. Since this was written patient P. T. had a sudden acute attack of bursitis of the same shoulder and was operated on, with immediate complete relief.

Immobilization of the shoulder, whether by swathe or by plaster encasement, is mentioned only to be condemned, because of the real danger of the formation of adhesions.

My practice has been to explain to each patient as simply as possible the underlying anatomy and pathologic condition and what my experience has been with the various modes of treatment. Choice of therapy is then left largely to the patient. The result has been that only a few patients ask for immediate operative relief. The majority decide to try heat applications, baking, diathermy or short wave. Some obtain complete relief after more or less prolonged treatment, but in most cases the relief is temporary or partial, with

17. Bartels, W. P.: Surgical Treatment of Acute Subacromial Bursitis, J. Bone & Joint Surg. **22**: 120-121 (Jan.) 1940. Hitzrot, J. M.: Surgical Diseases of Bursae, Ann. Surg. **98**: 273-282 (Aug.) 1933. Weiland, A. H., and Burbacher, C. R.: Bursitis, South. Surgeon **9**: 26-33 (Jan.) 1940. Carnett and Case.[16] Codman.[15] Haggart and Allen.[13] Wilson.[34]

18. Patterson, R. L., Jr., and Darrach, William: Treatment of Acute Bursitis (Subdeltoid) by Needle Irrigation, J. Bone & Joint Surg. **19**: 993-1002 (Oct.) 1937.

19. Dickson, J. A., and Crosby, E. H.: Periarthritis: Analysis of Two Hundred Cases, J. A. M. A. **99**: 2252-2257 (Dec. 31) 1932. Mumford and Martin.[5]

20. Lattman, Isidore: Treatment of Subacromial Bursitis by Roentgen Irradiation, Am. J. Roentgenol. **36**: 55-60 (July) 1936. Loewnecken, R.: Roentgenotherapy of Humero-Scapular Peritendinitis, Med. rev. Bergen **40**: 499-507 (Nov.) 1932. Segre, M.: Roentgenotherapy of Calcareous Scapulo-Humeral Periarthritis, Radiol. méd. **23**: 522-539 (July) 1936. de Lorimier.[8] Mustakallio.[4]

recurring attacks over a period of years. Six patients have returned for excision of the deposit.

While I feel that large deposits should be excised regardless of symptoms, to forestall the development of an acute attack of bursitis, no patient has yet been willing to have this done. Medium and tiny deposits should, in general, be treated conservatively and should be watched.

SUMMARY AND CONCLUSIONS

Among 6,061 supposedly normal persons of the white collar class, calcium was found on routine fluoroscopic examination in one or both shoulders of 165 (2.7 per cent). Of this series 5,061 were studied at annual intervals over a three year period and provide the material from which the following conclusions are drawn:

1. Fluoroscopy and spot-film roentgenography are invaluable aids in the detection and precise localization of calcium deposits in the shoulder.

2. Calcium deposits occur most commonly during the period of greatest activity of adult life, and especially among males.

3. Serious illness, arthritis, rheumatism and infection, whether local or systemic, past or present, exert no influence on the formation or regression of deposits.

4. Occupations that require constant prolonged abduction of the arms foster the formation of calcium deposits in the shoulder.

5. A single trauma per se does not cause calcium deposition, although it is occasionally associated with the onset of an inevitable bursitis.

6. Although fluoroscopically visible calcium deposits may form within as short a period as two months, most deposits require a considerably longer time for their formation.

7. Medium and tiny deposits may disappear without symptoms, but large deposits always result in a painful shoulder sooner or later, though they may remain quiescent and symptomless for months or years.

8. Excision of the deposit is recommended as the best treatment for the acute attack, since it offers immediate, certain, complete and permanent relief.

1045 Park Avenue.

A Liberal Profession.—Medicine today is probably the most liberal of all the professions of society. It recognizes addition to its knowledge from any source, and the present edifice of scientific medicine has been reared on the labor and contributions of innumerable physicians, scientists and lay people, regardless of race, color or creed. Medicine is the most international of sciences and therefore least nationalistic. It comprises a democracy of intelligence, knowing neither geographic nor racial bounds. Medicine has no bench or bar; the lawyer must pay deference to the judge, who intellectually may be his inferior; neither has medicine a hierarchy as in the case of the ecclesiastical profession. In medicine all men are alike; there are no castes, no orders, no class distinctions. Its devotees meet on common ground in practice, in research, in hospitals, in schools and in conventions, where eager minds come together for mutual improvement and understanding. . . . Medical science has done much to make possible the state of society as it exists today.—Abell, Irvin: The Spirit of Medicine, *Pharos of Alpha Omega Alpha*, May 1941.

CENTRAL NERVOUS SYSTEM MANIFESTATIONS OF INFECTIOUS MONONUCLEOSIS

REPORT OF A CASE

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JOSEPH P. REICH, M.D.
AND
SAMUEL PERLOW, M.D.
CHICAGO

Involvement of the central nervous system in infectious mononucleosis is rare, but probably not as rare as the dozen or so cases thus far reported would seem to indicate. What is more likely is that the nervous system involvement so masks the other manifestations of the disease that the diagnosis is overlooked.[1] The nervous symptoms may appear as much as two weeks before the characteristic lymphadenopathy and splenic enlargement [2] resulting, if the characteristic blood picture is overlooked, in the erroneous diagnosis of lymphocytic choriomeningitis, acute toxic encephalitis, epidemic encephalitis or early poliomyelitis.

The neurologic symptoms produced may be multiple. All patients have headaches. There is a varying degree of dulling of the sensorium from mild lethargy to coma. The patient may be irritable and irrational.[3] There may be photophobia, nystagmus and poor articulation.[3] Peripheral neurologic symptoms, such as facial nerve palsy, oculomotor nerve involvement, optic neuritis and anosmia, are occasionally present. Signs of meningeal irritation are usually present with positive Kernig and Brudzinski signs, nausea and vomiting.

The spinal fluid has been examined in only a few cases, and the conditions found are neither characteristic nor constant. The pressure may or may not be moderately elevated. Pleocytosis is variable, usually from 25 to 300 cells, largely lymphocytes. On one occasion a cell count over 1,000 was reported.[4] In our case the cell count at the height of the disease was normal. The total protein may be increased, as may the globulin fraction. The spinal fluid Wassermann reaction and colloidal gold curves are negative. Schmidt and Nyfeldt [5] and Huber [4] found abnormal spinal fluids in several cases of infectious mononucleosis in the absence of any nervous system symptoms or signs. Schmidt and Nyfeldt [5] were also able to obtain cultures of Listerella from the spinal fluid in 4 of 5 cases. Cerebral symptoms were present in only 1 of these cases.

Characteristically the nervous system symptoms and signs disappear, with no residuum. The spinal fluid returns to normal some time after the symptoms and signs disappear.[3]

REPORT OF CASE

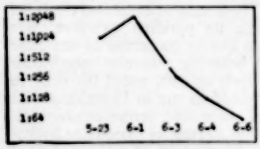
B. S., a white man aged 21, was admitted to the Michael Reese Hospital on May 19, 1940 complaining of severe headache, dizziness, vomiting and a staggering gait of one week's duration.

From the Michael Reese Hospital.

1. Epstein, S. H., and Dameshek, William: Involvement of the Central Nervous System in a Case of Glandular Fever, New England J. Med. **205**: 1238, 1931.
2. Goe††, O.: Serous Meningitis in Pfeiffer's Glandular Fever (Infectious Mononucleosis), Deutsche med. Wchnschr. **63**: 1759, 1937.
3. Marshall, E. A.: Infectious Mononucleosis, Am. J. Clin. Path. **9**: 298, 1939.
4. Huber, W.: Serous Meningitis in Pfeiffer's Glandular Fever, Schweiz. med. Wchnschr. **68**: 892, 1938.
5. Schmidt, V., and Nyfeldt, A.: Regarding Infectious Mononucleosis and Meningoencephalitis, Acta oto-laryng. **26**: 680, 1938.

He was well until approximately ten days before admission, when he had severe pain in his calf muscles lasting one day. On the following day the pain subsided, but dizziness and headache began, which gradually became more severe, especially while he was in the erect position. His gait became very unsteady. Frequent attacks of nausea and vomiting followed. Five days before he entered the hospital these symptoms became so severe that he was obliged to stay in bed. The patient was very irritable at first but later became more and more lethargic, and at times responded irrationally. He complained bitterly of the headaches, which were retro-orbital and frontal. His temperature during the week prior to admission rose to 101 F. during the evening but fell to 99 in the morning. There was no history of a sore throat, cold or cough in the recent past. The past history and family history were noncontributory. He was employed in a fruit commission house where only California fruit was handled. There was no history of insect or animal bite or of head injury.

On physical examination the patient appeared well nourished and lay quietly in bed, exhibiting but little interest in his surroundings. The temperature was 100 F. and the pulse rate 100 per minute. The skin showed no petechiae, ecchymoses or eruptions. It was warm, and perspiration was profuse. The conjunctivas showed no petechiae or icterus. The extraocular muscles were normal. There was no nystagmus. The pupils reacted normally to light and in accommodation, were equal in size and were regular. The fundi were normal. The tongue was heavily coated and dry. There were several carious teeth. The mucous membrane of the pharynx was not injected. The tonsils were absent. There was no cervical adenopathy. The lungs and heart were normal. The abdomen was soft and not tender. No masses were palpable. The spleen, liver and kidneys were not palpable. There was no cyanosis or edema of the extremities or axillary, epitrochlear or inguinal lymphadenopathy.



Blood heterophile agglutination titer.

Neurologic examination revealed a freely movable head and no neck rigidity. The head was not tender on percussion. The eyes were normal. Likewise the other cranial nerves were intact. The speech was poorly articulated; the words were slurred, somewhat explosive in character and often hardly understandable. Reading aloud exaggerated these peculiarities. The ability to see the printed words did not seem impaired. Muscular movement, tone and strength were normal. However, the muscular coordination was very poor. In the finger-to-nose test the nose was missed consistently, and the movement was not smooth but was broken up into several stages. In the heel-to-knee test the heel was brought to the knee fairly accurately, but when the patient was directed to leave it there or to slide the heel downward along the tibial crest the foot shook violently, and there was extreme unsteadiness and deviation. Standing was possible only with the legs spread widely apart, and even then there was pronounced swaying. When the feet were brought together the patient tended to fall backward. Walking was extremely unsteady and almost impossible. Sensation was normal for touch, pinprick, movements and vibration. Reflexes were normal except for a more vigorous radial jerk, absent left cremasteric and absent cutaneous abdominal reflexes. The knee jerks and ankle jerks were normal. The Babinski reflex was absent.

The patient was slow in understanding and almost stuporous. Occasionally one had to speak to him loudly to maintain his attention. He attempted to cooperate but followed directions very poorly. His answers were very slow in forthcoming, but fairly reasonable. When the patient's extremities were placed in the most uncomfortable positions, he tended to maintain that position in almost catatonic manner. His face was devoid of expression.

The impression at this time was that we were dealing with an encephalomyelitis secondary to some unknown systemic infection. The patient's symptoms remained unchanged on May 20 and 21 but began to improve on the 22d and continued improving until his discharge. The high mononuclear count (50 per cent) present on the day following admission provoked comment, but it was not until the laboratory reported a blood heterophile agglutination titer of 1:1,024 that its significance became clear. Reexamination of that blood film and all subsequent blood films demonstrated the typical blood picture of infectious mononucleosis (table 1). There was a high lymphocyte percentage. The lymphocytes showed much variation in size. The nuclei were darkly stained and contained many vacuoles. There was a shift to the left among the granulocytes, with many unsegmented cells. There were also many disintegrating and degenerate neutrophils. The frequently repeated blood studies (table 1) show the gradual decrease in monocytes and large lymphocytes as recovery progressed. A stool passed on the 20th was reported having 3 plus occult blood. For this reason bleeding, coagulation and prothrombin times were determined and found normal (1 minute 10 seconds, 3 minutes five seconds and 30 seconds respectively). The platelet count was 220,000 per cubic millimeter.

TABLE 1.—*Blood Counts*

	5/19	5/20	5/21	5/25	5/29	5/31	6/2	6/3	6/4	6/6
Erythrocytes	..	5.98	..	5.1	..	..	5.5	..	..	..
Hemoglobin, %	..	80-90	..	80	..	80-90	90(S)	..	..	..
Leukocytes	13,600	11,400	13,800	14,600	11,300	11,150	10,400	10,100	8,300	8,100
Neutrophils, %	..	50	..	12	..	23	19	22	35	51
Lymphocytes, %	..	39	..	88	..	66	71	69	52	44
Large lymphocytes	..	..	..	28	..	..	40	27	..	12
Small lymphocytes	..	..	..	60	..	..	31	42	..	32
Monocytes	..	11	..	..	..	11	10	9	9	4
Wassermann reaction	..	Neg.	..	Neg.	..	..	Neg.	Neg.	Neg.	Neg.
Kahn reaction	..	Neg.	..	Neg.	..	..	Neg.	Neg.	Neg.	Neg.

It is interesting that careful reexamination each day after the nature of the illness was recognized failed to reveal enlarged lymph nodes until May 31 (twelve days after the patient entered the hospital and twenty-two days after the onset of symptoms), when several large glands were found in the neck and a chain of large glands appeared in both inguinal regions. Later the axillary nodes became enlarged. On June 3, twenty-five days after the onset of the illness, the spleen became palpable on deep inspiration.

TABLE 2.—*Spinal Fluid*

	5/20	6/1	6/5
Culture	Negative	Negative	Negative
Cells	5 lymphocytes	9 lymphocytes	1 lymphocyte
Pandy	+	+	Ft. tr.
Ross-Jones	+	+	Ft. tr.
Total protein, mg. per 100 cc.	156	170	77
Dextrose, mg. %	46	45	41
Wassermann	Negative	Negative	Negative
Colloidal gold	Negative	Negative	Negative
Heterophile	..	Negative	Negative
Pressure, mm.	175	132	158

Table 2 shows the spinal fluid findings. Fluid drawn the day following admission was found to have a normal cell content with a considerable increase in the total protein content and the globulin fraction. Fluid drawn on June 1, after almost all the neurologic abnormalities had disappeared, showed almost the same high protein level and a slightly elevated count. Fluid drawn on June 6, the day before the patient was discharged and after he had been symptom free for more than a week,

showed a greatly reduced but still elevated protein content. The Pandy and Ross-Jones tests were only slightly positive. The cell count was normal.

We have read no reports of spinal fluid examination for heterophile agglutinins in infectious mononucleosis. Serial dilutions beginning with 1:4 concentrations revealed no such agglutinins in our case. Blood and spinal fluid cultures remained sterile.

The chart shows the rapid fall in blood heterophile agglutinins during recovery to an almost insignificant degree just prior to the patient's discharge from the hospital.

Agglutination tests of the patient's serum against Listerella monocytogenes were negative. Throat cultures made on the day of admission showed only alpha streptococci. The urine was constantly normal.

COMMENT

This case is almost unique among the cases of infectious mononucleosis which showed involvement of the central nervous system, in that there were no signs and almost no cerebrospinal abnormalities (except for 9 cells in one count) pointing to meningeal involvement. Especially striking was the cell protein dissociation in favor of the protein, which speaks against involvement of the meninges. In the majority of the cases reported there was meningeal involvement with a considerable increase in cell content, at least during one phase of the disease, while the protein showed hardly any increase.

Only one case has been reported [6] in which the symptoms (paresis of the left inferior rectus muscle of the eye, highly exaggerated knee jerks, a questionable plantar reflex and entirely normal cerebrospinal fluid) pointed to a purely encephalitic process.

In our case the cerebral involvement was much more extensive. The clinical picture was that of an acute ataxia with outspoken involvement of the cerebellar system.

This is not the place to discuss at any length the question of the localization of the acute ataxia, whether it is produced by the toxi-infectious process of the coordination system (Davidenkoff) or by a circumscribed focus in the hypothalamic region (Margulis). It seems, however, that the pathologic process, whether it is a real "encephalitis," i. e. an inflammatory process, or a "toxic encephalopathy," extends over a rather large area of the brain. In our opinion there cannot be any doubt about the involvement of the cerebellar system. On the other hand there were a number of signs (expressionless face, lack of motor impulse, peculiar kind of somnolence, diffuse perspiration) which make one think of a pathologic process in the gray matter surrounding the third ventricle, the hypothalamic region, so that the possibility of a lethargic encephalitis was considered for a short time.

It is interesting that the lymphadenopathy and palpable spleen, the usual and characteristic signs of infectious mononucleosis, did not appear until the alarming cerebral symptoms were almost gone. We must admit that the diagnosis would have probably been missed except for the laboratory report of positive blood heterophile agglutination, and the case would have been relegated to that wholly unsatisfactory waste-basket category of "aseptic" or "toxic encephalitis." We feel, therefore, that in the presence of acute cerebral symptoms of unknown etiology the heterophile agglutination test should be made.

Several workers have reported isolating Listerella in infectious mononucleosis. Schmidt and Nyfeldt were able to obtain cultures of the organism from the spinal fluid in 4 of 5 cases of the disease, in only 1 of which were cerebral symptoms present. In our case three attempts at obtaining cultures of the organism were unsuccessful.

The spinal fluid in our case was negative for heterophile agglutinins.

SUMMARY

1. In a case of infectious mononucleosis the only early symptoms simulated those of encephalitis.

2. The heterophile agglutination determination is of value in cases in which acute cerebral symptoms of unknown etiology are present.

6. Fledelius, M.: Paresis of Eye Muscles as Complication of Infectious Mononucleosis, Acta ophth. **13**: 150. 1935.

TREATMENT OF PARALYSIS AGITANS WITH VITAMIN B_6 (PYRIDOXINE HYDROCHLORIDE)

A. B. BAKER, M.D.

MINNEAPOLIS

Pyridoxine hydrochloride, or the vitamin B_6 fraction of the vitamin B complex, was first discovered by György [1] in 1935 and was first prepared synthetically in 1939 by Harris and Folkers.[2] It consists of 2-methyl-3 hydroxy-4, 5-dihydroxy-methyl-pyridine. It was first used clinically by Antopol and Schotland [3] with beneficial results in 6 patients with pseudohypertrophic muscular dystrophy. These authors expressed the belief that the drug, through its pyridine structure, was involved in the enzyme system concerned in muscular metabolism. Jolliffe,[4] believing muscular metabolism to be involved in paralysis agitans, tested the drug in this condition. He reported its use in 15 patients with paralysis agitans, all of whom had severe involvement. All patients received 50 to 100 mg. of pyridoxine hydrochloride intravenously. Four of the 15 patients showed definite objective improvement. The best results occurred in the idiopathic or arteriosclerotic type of the disease.

Since a considerable proportion of the patients visiting the Outpatient Clinic of the University of Minnesota Hospitals suffer from paralysis agitans, the staff naturally was most anxious to obtain and try any new therapeutic agent that might offer possible aid to these unfortunate persons. A group of 15 patients suffering from paralysis agitans were, therefore, selected for intravenous therapy with pyridoxine hydrochloride.

The type of patient, the amount of treatment and the results of the therapy are shown in the accompanying table. Nine obtained only two weeks of treatment at daily intervals; 6 of these received only 50 mg. of pyridoxine hydrochloride; 2 received 50 mg. for one week and 100 mg. during the second week, while 1 received 100 mg. for two weeks, supplemented by 54 grains (3.5 Gm.) of brewers' yeast. Three patients showed definite objective improvement (in cases 1, 10 and 12). Of these, 1 had idiopathic parkinsonism and 1 had postencephalitic involvement, while the condition

From the Division of Nervous and Mental Diseases, University of Minnesota Medical School.

The vitamin B_6 used in these studies was hexabion hydrochloride, furnished by Merck & Co., Inc.

1. György, Paul: Investigations on the Vitamin B_2 Complex: The Differentiation of Lactoflavin and the "Rat Antipellagra" Factor, Biochem. J. **29**: 741, 1935.

2. Harris, S. A., and Folkers, K.: Synthetic Vitamin B_6, Science **89**: 347 (April 14) 1939.

3. Antopol, William, and Schotland, C. E.: The Use of Vitamin B_6 in Pseudohypertrophic Muscular Dystrophy, J. A. M. A. **114**: 1058 (March 23) 1940.

4. Jolliffe, Norman: Clinical Aspects of Vitamin B Deficiencies, Minnesota Med. **23**: 542 (Aug.) 1940.

of the third patient, although she offered no history of any previous illness, suggested postencephalitis, since the age at onset was 39.

Six patients received daily intravenous treatment with pyridoxine hydrochloride for three or more weeks. This treatment was supplemented with the whole vitamin B complex in the form of 54 grains daily of brewers' yeast. In 5 of these patients the illness was idiopathic, while in 1 it was postencephalitic. Three patients, all of whom had idiopathic parkinsonism, showed definite objective improvement. Neither the age of the patient nor the duration of symptoms seemed to have any effect on the treatment. Good results were obtained in persons whose illness had been present for as long as fifteen years, while often no improvement occurred in some whose illness was fairly recent. The most favorable results appeared in the idiopathic type of the disease. This is in agreement with the results reported by Jolliffe.[4] The nature of the improvement varied from patient to patient. In some it consisted of a drastic reduction in the severity of the tremor; in others the tremor was only slightly affected while the rigidity improved, allowing the patient more freedom in movement. All the patients benefiting from the drug reported a definite subjective improvement, consisting of a decreased fatigability, better sleeping and increased appetite. One patient had gross choreiform movements rather than a parkinsonian syndrome. Since the involvement probably was arteriosclerotic and also extrapyramidal, it seemed of interest to attempt therapy with pyridoxine hydrochloride. Her improvement was most striking, suggesting the possibility that this type of therapy may be of benefit in other types of extrapyramidal involvement. A brief report of those patients responding to this therapy will aid in evaluating the results.

REPORT OF CASES

CASE 1.—E. C., a woman aged 67, first noticed a definite tremor and rigidity of her hands in 1935. The involvement gradually spread to almost all the muscles of her body, including the muscles of the trunk, producing at first a shuffling gait and mild postural changes and finally an almost complete invalidism, the patient ultimately being confined to a wheel chair. She became weak and for years was able to sit up only for short periods. She had difficulty in sitting up in a car during even a short ride. She had been treated with scopolamine hydrobromide but showed no response to this type of therapy.

Neurologic examination revealed a moderate tremor and extreme rigidity of all limbs. There was complete loss of facial expression and an absence of blinking. The patient was unable to walk or stand without aid. The deep reflexes were reduced but equal. The rest of the examination gave negative results.

She was given daily intravenous injections of 50 mg. of pyridoxine hydrochloride for one week and 100 mg. for the second week. Improvement became apparent after three weeks. Expression rapidly returned to the patient's face. Her tremor became reduced and at times would be completely absent, even under emotional excitement. The rigidity also diminished, so that the patient was soon able to sit up for long periods of time and was also able to walk about the house unassisted. Long rides and even the entertaining of company no longer fatigued the patient.

She has continued to maintain her improvement in spite of two severe gastrointestinal upsets.

CASE 6.—L. S., a man aged 47, a jeweler, in 1935 first became aware of an impairment in speech associated with a generalized bodily weakness. He described this weakness as a general slowing down of all his activities, primarily because of difficulty in using his muscles. Impairment in speech consisted in difficulty in getting words out and a gneral running together of his words as they came out. The muscular rigidity became more severe, retarding all his voluntary movements. Because of this difficulty he soon became unable to carry on his work as a jeweler. His writing became impaired and his facies expressionless. Continuation of his illness finally resulted in the patient's complete inability to do any type of work.

The neurologic examination revealed a dysarthria and dysphonia associated with a masklike facies and a generalized muscular rigidity. Tremor was not present. Laboratory tests all gave negative results. The patient was placed on varying doses of scopolamine hydrobromide, which he continued to take for a period of months with no improvement. He was then given two courses of pyridoxine hydrochloride intravenously, separated by a two week interval. The first consisted of 50 mg. of the drug daily for a period of two weeks, the second of 50 mg. daily for one week followed by 100 mg. doses the second week. He was simultaneously given 54 grains of brewers' yeast daily. After the second week of his first course of treatment, the patient began to notice definite improvement in his speech. His voice lost part of its monotonous character and there was a definite ability to phonate better. After three weeks of treatment, his facial expressions became livelier. Improvement continued. The muscular rigidity became so reduced that the patient was able to play ball and perform much of the work which he had been forced to discontinue prior to his treatment. At present he is taking 20 mg. weekly of pyridoxine hydrochloride given orally and has maintained his striking improvement.

CASE 7.—A. G., a man aged 54, first noticed a slight stiffness in his left arm and leg in 1927. This rigidity gradually increased, producing a definite difficulty in gait. Three months after the onset of rigidity a coarse tremor appeared in the left hand and soon extended to the entire extremity but has always remained more or less localized to the left upper extremity. One year later there appeared an involvement of the facial muscles and a slight disturbance in speech. There was no history of any severe infectious process antedating the onset of his present illness.

Neurologic examination revealed a slight masking of the facies and a moderate sialorrhea. There was rigidity involving all extremities, being most noticeable on the left side, with a tremor limited to the left upper extremity. The patient had difficulty in performing both fine and gross movements with his hands. Scopolamine hydrobromide, which he had taken for a number of years, had produced but little improvement. During the past eight or nine years of his illness his condition had been more or less stationary.

He was given daily intravenous injections of pyridoxine hydrochloride, receiving a total of four weeks of treatment with 100 mg. of the medication. At the same time he was given 54 grains of brewers' yeast daily by mouth. After the completion of his treatment, the patient noticed a definite decrease in the tremor of his left upper extremity. His rigidity became reduced, and his impairment in speech completely disappeared. Whereas before the patient was able to walk for only short distances without becoming tired, he could now walk with ease for many blocks. He was given 40 mg. of pyridoxine hydrochloride by mouth weekly and in three months showed no recurrence of the involvement.

CASE 10.—C. S., a woman aged 54, first noticed a tightness of her legs in 1925. One year later there developed a mild tremor of her right hand associated with definite rigidity. This involvement remained localized to the lower limbs until 1938, at which time it spread rapidly to the other extremities. The progress of the illness had been rapid during the past few years, resulting in a slow and shuffling gait and a severe and annoying tremor in her arms. She had continued to walk and travel about unassisted, although she had refused to go out in company because of her condition. More recently a moderate sialorrhea and some scanning of her speech developed. The patient gave no history suggesting any previous involvement of the central nervous system, although her age at onset certainly was suggestive of a postencephalitic involvement.

Examination revealed the characteristic parkinsonian syndrome. The facies was expressionless, and blinking was infrequent. The impairment in speech was noticeable. There was considerable rigidity of all extremities, associated with a rapid,

shuffling gait. A severe tremor was present in the upper limbs and there were beginning contractures of the hands.

She was given a single course of daily intravenous injections of 50 mg. of pyridoxine hydrochloride the first week and 100 mg. the second week. Along with this medication she received 54 grains of brewers' yeast by mouth. After this course of treatment she was given 40 mg. of pyridoxine hydrochloride by mouth weekly.

Improvement began a few weeks after her treatment. The tremor immediately subsided almost to the vanishing point. Her rigidity improved so that she was able to get around much better. Her improvement has been maintained on the oral medication.

CASE 12.—G. F., a woman aged 39, first noticed her illness in 1936, at which time she suffered a mild tremor of the upper extremities. About six months after the onset of the tremor there appeared a definite rigidity of the upper extremities, a noticeable disturbance in speech and severe sialorrhea. There was a general slowing up of all her activities, and her gait became shuffling. She found it impossible to do her housework or to carry out her regular activities. At the time of her examination she presented a masklike facies, a staring gaze and a severe tremor and rigidity of all the extremities. She had a definite shuffling gait, walking with small steps and finding difficulty in raising her extremities. She had been taking scopolamine hydrobromide, amphetamine sulfate and various other types of medication over a period of years, with little alleviation of her symptoms.

She was given daily intravenous injections of 50 mg. of pyridoxine hydrochloride, receiving treatment for two weeks. At the time of the completion of her treatment she showed no definite objective improvement. She was followed for a period of two months. Six weeks after the completion of treatment she began to improve. Her rigidity decreased to the extent that she was able to do her own housework and move about much better. The sialorrhea decreased remarkably, and her

Summary of Drug Therapy

Case No.	Patient	Age	Sex	Type of Paralysis Agitans	Duration of Disease, Years	Severity of Disease	Result of Treatment	Duration of Treatment, Weeks	Type of Medication	Daily Dosage
					A. Pyridoxine Hydrochloride Given Intravenously					
1	E. C.	67	♀	Idiopathic	5	Severe	Definitely improved	2	Pyridoxine hydrochloride Brewers' yeast	50 mg. 1 week 100 mg. 1 week 54 grains
2	G. F.	65	♂	Idiopathic	2	Moderate	Unimproved	2	Pyridoxine hydrochloride	50 mg.
3	C. M. J.	65	♂	Idiopathic	8	Severe	Unimproved	2	Pyridoxine hydrochloride	50 mg.
4	V. G.	59	♂	Idiopathic	5	Moderate	Unimproved	2	Pyridoxine hydrochloride	50 mg.
5	L. B.	59	♀	Idiopathic	15	Severe	Unimproved	3	Pyridoxine hydrochloride Brewers' yeast	100 mg. 54 grains
6	L. S.	47	♂	Idiopathic	5	Moderate	Definitely improved	4	Pyridoxine hydrochloride Brewers' yeast	50 mg. 3 weeks 100 mg. 1 week 54 grains
7	A. G.	54	♂	Idiopathic	13	Moderate	Moderately improved	4	Pyridoxine hydrochloride Brewers' yeast	100 mg. 54 grains
8	F. Z.	63	♂	Idiopathic	11	Severe	Unimproved	4	Pyridoxine hydrochloride Brewers' yeast	50 mg. 3 weeks 100 mg. 1 week 54 grains
9	I. M.	71	♀	Senile chorea	4	Severe	Definitely improved	3	Pyridoxine hydrochloride Brewers' yeast	50 mg. 1 week 100 mg. 2 weeks 54 grains
10	C. S.	54	♀	?	15	Moderate	Moderately improved	2	Pyridoxine hydrochloride Brewers' yeast	50 mg. 1 week 100 mg. 1 week 54 grains
11	M. F.	58	♀	?	16	Moderate	Unimproved	2	Pyridoxine hydrochloride Brewers' yeast	100 mg. 54 grains
12	G. F.	39	♂	Postencephalitic	4	Moderate	Moderately improved	2	Pyridoxine hydrochloride	50 mg.
13	B. H.	38	♂	Postencephalitic	5	Moderate	Unimproved	2	Pyridoxine hydrochloride	50 mg.
14	G. A.	49	♂	Postencephalitic	18	Severe	Unimproved	3	Pyridoxine hydrochloride Brewers' yeast	50 mg. 1 week 100 mg. 2 weeks 54 grains
15	L. B.	35	♀	Syphilitic	4	Severe	Unimproved	2	Pyridoxine hydrochloride Brewers' yeast	50 mg. 54 grains
					B. Pyridine Hydrochloride Given Orally					
16	A. C.	69	♂	Idiopathic	3	Severe	Definite subjective improvement; mild objective improvement	3	Pyridoxine hydrochloride Brewers' yeast	50 mg. 54 grains
17	J. C.	60	♂	Idiopathic	2½	Moderate	Subjective improvement only	3	Pyridoxine hydrochloride	50 mg.
18	J. V.	62	♂	Idiopathic	10	Severe	Unimproved	3	Pyridoxine hydrochloride Brewers' yeast	50 mg. 54 grains
19	A. J.	60	♂	Idiopathic	3	Moderate	Unimproved	3	Pyridoxine hydrochloride Brewers' yeast	50 mg. 54 grains

tremor became almost imperceptible. She still has slight difficulty in speech, although this has also improved.

CASE 9.—I. M., a housewife aged 71, had been afflicted for the past twelve years with gross, bizarre, purposeless, involuntary movements which began first in the arms and later spread to the rest of her musculature. For the past three years this involvement had totally incapacitated the patient. Walking had been almost impossible, and she had been unable to care for or feed herself. The patient's mother had been similarly afflicted but not to the degree to which the patient was involved. The patient has one brother, aged 67, who has noted similar mild twitchings during the past few years. The other five siblings are unaffected. She has three daughters who are at present unaffected. The physical examination, aside from the normal evidences of senescence, revealed no abnormalities. The neurologic examination revealed continuous involuntary, irregular movements involving the upper portion of the patient's trunk, arms and head. These choreiform movements also involved, but to a much less extent, the lower extremities, so that walking was difficult and her gait slightly bizarre. Laboratory studies all gave negative results. Fluoroscopic examination of the chest and a 6 foot roentgenogram of the heart gave negative results. The diagnosis in this case was senile chorea.

The patient was given ½ teaspoon (2 cc.) of a concentrated yeast (Anheuser-Busch) twice a day and pyridoxine hydrochloride intravenously daily in 50 mg. doses. The pyridoxine hydrochloride was increased to 100 mg. after the second week. These medications were discontinued after three weeks, and the patient was given 40 mg. of pyridoxine hydrochloride by mouth weekly. After the first few injections of the drug her condition showed improvement, which continued during the treatment. After three weeks the patient was walking unassisted and with ease, and her gait showed no observable abnormality. She was now able to write her own name. She could feed herself, but only with considerable difficulty. The choreiform movements were greatly reduced, and the patient could now sit quietly in a chair, whereas previously she had presented rather a bizarre picture. Subjectively the patient felt stronger. This manifested itself in an improved appetite and more restful sleeping.

COMMENT

Fifteen patients suffering from paralysis agitans were treated intravenously with pyridoxine hydrochloride, supplemented in most cases by the oral administration of brewers' yeast. The patients received 50 to 100 mg. of the intravenous medication at daily intervals for from two to four weeks. Nine patients had idiopathic or arteriosclerotic parkinsonism, and of these 4 were improved. One of these patients had senile chorea rather than true parkinsonism. This patient showed a most striking improvement, suggesting the possibility that therapy with pyridoxine hydrochloride may be of benefit in other types of extrapyramidal involvement. Of the remaining 6 patients, 2 showed improvement. In the latter group 3 had postencephalitic paralysis agitans and 1 the syphilitic form. In the remaining 2 patients the etiologic factors producing paralysis agitans were undetermined.

Four patients suffering from arteriosclerotic or idiopathic paralysis were treated orally with 50 mg. of pyridoxine hydrochloride daily for three weeks supplemented by 54 grains of brewers' yeast. Two of these patients insisted that improvement had occurred but in only 1 was there any objective benefit in the form of an observable decrease in the tremor and rigidity.

The small number of patients and the inadequate dosage do not allow any definite conclusions; however, the results with the oral medication are suggestive and have encouraged me to undertake further investigations with this method of administering pyridoxine hydrochloride, or vitamin B_6.

THE CEREBROSPINAL FLUID IN DELIRIUM TREMENS

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Drainage of the cerebrospinal fluid by means of spinal puncture as a therapeutic measure in delirium tremens was introduced by Steinebach [1] in 1915. In that same year Hoppe [2] introduced this procedure in the United States; since then the treatment has become highly popular. Although it is now generally assumed that an increase in intracranial pressure occurs in delirium tremens and that drainage of the cerebrospinal fluid will relieve that tension, few data in support of this hypothesis can be found in the literature.

In a series of 18 cases, Steinebach found 14 patients (75 per cent) to have an increased pressure of the cerebrospinal fluid. However, this conclusion was based on his interpretation of any pressure above 150 mm. of water as abnormally increased, which criterion is not in accord with that generally employed in this country, in which the upper limit of normal is usually considered to be 180 mm. of water.[3] All the pressures observed in his cases were not recorded by Steinebach and hence cannot be reevaluated. With no substantiating data, Hoppe also concluded that the pressure of the cerebrospinal fluid is "always increased in delirium tremens." [2] Similar conclusions without supporting data were made by Goldsmith [4] from studies on patients with alcoholic deliriums and other acute alcoholic psychoses, in which he claimed that in 48 per cent of his cases the cerebrospinal fluid "came out under considerable pressure." Likewise, Levinson [5] stated that in delirium tremens the "cerebrospinal fluid pressure is greatly increased, running as a rule from 150 to 300 mm. of water," but gave no data to support his conclusion. In a similar manner other authors,[6] in discussing the treatment of delirium tremens, have expressed the belief that an increase in intracranial pressure occurs, even though ample demonstration of such a phenomenon is still lacking.

The only study on delirium tremens which cast some doubt on the aforementioned general conclusion was that of Thomas, Semrad and Schwab.[7] These authors reported 40 cases of delirium tremens in 20 of which spinal puncture and drainage were done. In only 12 of their cases were readings of pressure reliable, but in all 12 the pressures of the cerebrospinal fluid were normal. In view of the small number of cases involved, these authors could not definitely negate the concept so generally accepted by others.

In view of the preceding reports, a review of the results obtained from examinations of the cerebrospinal fluid of patients with delirium tremens who were treated

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in the Psychiatric Pavilion of the Cincinnati General Hospital during the past four years was considered to be of value.

The records of 234 patients with delirium tremens admitted to the Psychiatric Pavilion of the Cincinnati General Hospital during the past four years were reviewed for this study. In order to keep the problem unobscured, all cerebrospinal fluids which were contaminated by blood as a result of a traumatic tap or an injury to the head and all fluids which reacted positively to the Wassermann test were excluded from the series.

The punctures were performed in the lumbar region with the patient in the lateral recumbent position. Pressures were measured with the Fremont-Smith modification of the Ayer water manometer. All readings of pressure were discarded unless the patient was relaxed and the measured pressure was a reliable one. The cells were counted in a blood-counting chamber. The majority of the cell counts were made by the glacial acetic acid method, although in the last year Unna's polychrome methylene blue was used for staining the cells prior to counting. The protein determinations

TABLE 1.—*Pressure of the Cerebrospinal Fluid in Patients with Delirium Tremens*

Pressure, Mm. of Water	Number of Patients	Percentage
Less than 180	154	73
180 to 200	26	12
200 to 300	26	12
300 to 400	5	3
Total	211	100

TABLE 2.—*Protein Content of the Cerebrospinal Fluid of Patients with Delirium Tremens*

Protein Content, Mg. per 100 Cc.	Number of Samples	Percentage
10 to 20	56	30
21 to 45	123	67
46 to 75	5	3
Total	184	100

were made according to the Ayer, Dailey and Fremont-Smith [8] modification of the Denis and Ayer method. The colloidal gold test was done according to the method of Lange, as described by Cockrill.[9]

RESULTS

Pressure.—Reliable readings were obtained in 211 cases (table 1). The pressure of cerebrospinal fluid was less than 180 mm. of water in 154 (73 per cent) and above 180 mm. in 55 (27 per cent). In only 5 cases was the cerebrospinal fluid pressure above 300 mm. of water.

Protein.—Protein determinations were made on 184 samples of fluid. They were below the accepted upper limits of normal, namely 45 mg. per hundred cubic centimeters of fluid, in 179 instances (97 per cent) and greater than 45 mg. in 5 instances (3 per cent) (table 2). There were 56 samples of fluid which had low values, being below 20 mg.

Cells.—Cell counts were recorded on 178 samples of fluid. The count was 5 cells per cubic millimeter or below in 168 fluids (94 per cent), between 6 and 10 cells per cubic millimeter in 7 (4 per cent) and above 10 cells (the highest being 17 cells per cubic millimeter) in 3 (2 per cent). The cells were all lymphocytes.

Colloidal Gold Test.—The colloidal gold reaction was determined on 55 samples of fluid and was normal in all of them. For the purpose of this report a reading of less than 2 (lilac) in any tube is reported as a negative reaction.

COMMENT

This study indicates that only 25 per cent of patients with delirium tremens have an abnormally high pressure of the cerebrospinal fluid. The vast majority of our patients had a normal pressure, thus invalidating the generalization that there is an increase of pressure in delirium tremens. If one considers that it is difficult to relax properly the patient with delirium tremens for accurate determination of the pressure of the cerebrospinal fluid even under the most favorable conditions, then the probability is enhanced that more than 75 per cent of such patients will have normal pressures.

These observations agree with those of Merritt and Fremont-Smith,[3] who examined the cerebrospinal fluid of 108 patients with acute alcoholic intoxication and found normal pressures in 75 per cent of the series. Likewise, Rosenbaum, Herren and Merritt [10] found normal pressures in 75 per cent of a series of 201 patients suffering with acute alcoholism (including, but not limited to, patients with delirium tremens).

In the aforementioned study by Rosenbaum, Herren and Merritt, about 20 per cent of the series had a slightly increased protein content in the cerebrospinal fluid. However, in the present study only 5 patients (3 per cent) had an increased concentration of protein in the cerebrospinal fluid. This apparent discrepancy probably is due to the fact that the patients in this series had had drainage of the cerebrospinal fluid with an average removal of 35 cc., while the patients examined by Rosenbaum, Herren and Merritt had had diagnostic taps only, with about an average removal of 10 cc. of cerebrospinal fluid. The protein content of the cerebrospinal fluid may be lower in the present series because the cerebrospinal fluid was diluted by ventricular fluid. This finding agrees with the well known fact that the protein content of cerebrospinal fluid varies with the site from which it is taken, the upper limits of protein in ventricular fluid being 15 mg., in cisternal 25 mg. and in lumbar 45 mg.[3]

The fact that the present study reveals the cerebrospinal fluid to be normal in the vast proportion of patients with delirium tremens does not preclude the advisability of performing spinal taps in such cases. The therapeutic advantages of such taps are doubtful,[11] but the diagnostic advantages are made apparent by the fact that in 7 cases in this series the diagnosis of an injury to the head was made in this manner. Adequate examination of spinal fluids revealed the presence of syphilis of the central nervous system in another 7 cases. Hence spinal taps are advocated for diagnostic purposes and not on the basis of reducing a hypothetical increased pressure of the cerebrospinal fluid.

CONCLUSION

The cerebrospinal fluid is normal in 75 per cent of patients with delirium tremens.

Burnet and Goodman streets.

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Clinical Notes, Suggestions and New Instruments

MAGNIFICATION OF SPERMATOZOA BY MEANS OF THE ELECTRON MICROSCOPE

PRELIMINARY REPORT

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Progress in physics and chemistry governs the development of modern medicine. From the time of Leeuwenhoek and his first successful microscope in the seventeenth century, man has been slowly penetrating deeper into the secrets of nature. It is a long cry from Leeuwenhoek's microscope to the binocular microscope with magnifications of 900, 1,500 and 2,000 diameters. Today we are on the eve of amazing discoveries which, in their importance and significance, rival those of William Harvey and Pasteur. The science of medicine is being revolutionized daily. Molecules which not long ago were theoretical entities are now clearly visualized by the electron microscope.

The ordinary refractive microscope revealed nothing more concerning the morphology of spermatozoa than the contour of the head and number and approximate length of tails. All the finer details were hopelessly concealed. Fundamentally, we know little about spermatozoa, and that little may be summed up as (1) motility or nonmotility, (2) general appearance of spermatozoa as seen with magnifications under 2,000 and (3) the numbers of spermatozoa per cubic centimeter of volume of semen. These observations were at one time the only criteria available. It is hardly feasible to think that by looking down from a mountain top into a valley many miles distant one may discern the features of the people and animals inhabiting it. Spermatozoa have presented just such a problem.

For many years it was assumed that motile spermatozoa were fertile. This assumption has since been discredited. Some authors have represented the body of the spermatozoon as being absent, just a head and a tail. Others have stretched their imagination to draw complicated spirem arrangements in the midsections. To obtain the photographs the following method was used:

In order to photograph a specimen through the electron microscope the specimen must be placed in a vacuum. It is therefore necessary to give this specimen added support to avoid disintegration. The microscope is operated with a current varying from 30,000 to 60,000 volts. The specimen of semen from which a spermatozoon was examined and photographed (which photographs are here reproduced) was 0.5 cc. in volume. This was placed in an ordinary test tube and diluted with distilled water to 15 cc. One drop of this specimen was then placed on a fine wire mesh screen, the wire being $\frac{1}{1000}$ inch in diameter. This screen was previously prepared in the following manner:

In a reservoir of distilled water having an outlet in the bottom center, the tiny film of collodion was floated. A small piece of screen mesh was placed over the opening. After a few minutes, in which time the collodion evaporated, the water was very carefully siphoned from the glass dish and the collodion film rested on the mesh. The specimen was then ready to be introduced into the vacuum chamber of the microscope. It is interesting to note that the collodion supports the specimen in such a manner that it can be photographed or observed "for periods of from five weeks to three months." The magnification of the original photograph from which figure 1 was reproduced was 13,500 diameters, and of figure 2, 27,000. The pictures were taken on March 31. There are a number of points of interest which can be seen at these magnifications.

This is offered as a preliminary report, made possible through the courtesy of the R. C. A. Electronic Research Laboratories with the help of Dr. Zworykin and Dr. Ramburg and the Cooperation of Mr. Pipper, Mr. Rhea, Mr. Volino and Mr. Ray.

The patient whose spermatozoa have been magnified through the electron microscope is a normal man of 32, the father of four children, the youngest being 6 months of age. It may be assumed, therefore, that the spermatozoon here illustrated is fertile and has been observed by the ordinary microscope at a magnification of 900 diameters. The motility was of high index and the longevity was eighteen hours. It can be further concluded that the spermatozoon was what is considered normal.

Human spermatozoa at this magnification in the electron microscope are so large that to photograph one spermatozoon it is necessary to take three separate pictures. This was accomplished by moving the slide while observing the spermatozoon through a large fluorescent screen in the viewing chamber. The magnification may then be adjusted to the desired value. The definition obtained in the small negative is sufficiently fine to allow enlargement up to any magnification desired. Figure 1 is a composite picture taking in the whole spermatozoon after reconstruction from three separate and distinct photographs. Figure 2 is the head and neck.

Measurements taken from a photographic enlargement are given solely for the purpose of showing the ratio of the different parts:

Head: Width at widest part, 7 cm. (from vertex to neck 11 cm.).

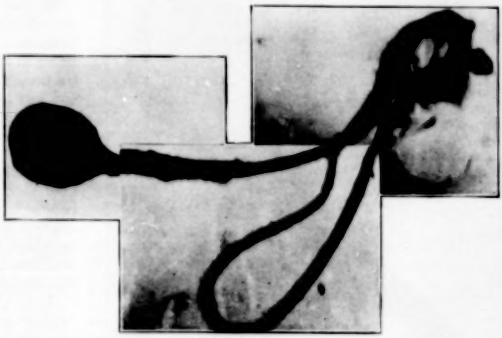

Fig. 1.—Human spermatozoon as viewed with the electron microscope. The original from which this illustration was reproduced was magnified 13,500 diameters. This is a composite of three separate pictures.

Body: Length, from neck to tail, 12 cm.

Tail: Length, from body to what appears to be the termination of the tail, 112 cm.

The head is shaped like a pear. The vertex presents a crater-like notch. The structure within this notch is somewhat less opaque than the main structure of the head, which is completely opaque down to where it vignettes into the body of the spermatozoon. Around the lower end of the "pear" appears a spongelike substance which is contiguous with a similarly appearing structure which runs along the entire length of the body.

The body appears to be a segmented structure, averaging nine to twelve segments in the specimens examined. This body of the spermatozoon is probably the structure, which under the refractive microscope appears as a narrow strip and which was known as the neck. Throughout the length of the body runs a core which is approximately uniform in diameter. This core is distinguished from the rest of the body by its opacity, being denser than the segmented structure around it. The core becomes the tail.

The core of the body surrounded by a narrow margin of substance, similar in opacity to the substance of the body segments, constitutes the tail. On the composite photograph, for a length of approximately 20 cm. from a point where the body terminates, the degree of opacity is apparently uniform.

The opacity then begins gradually to lighten for an approximate distance of 9 cm., where the opacity increases in density over a distance of approximately 9 cm., where it again becomes less dense and continues so throughout the remaining length of the tail. A delicately denser core runs through the length of these two lighter areas, which also show several small, dense, isolated buckshot-like bodies. The tail does not terminate abruptly but breaks up into a blurred, nondescript smudge.

In view of the number of details as revealed in a spermatozoon magnified 27,000 diameters by means of the electron microscope, opening up as this does an entirely new field of experimental research, it can be safely predicted that future investigations will undoubtedly clear up old problems, change our present conceptions of them and create new ones of which we now at present are totally unaware.

The apparent segmentation of the body probably accounts for the extraordinary motility of the head of the spermatozoon as it is propelled in a forward movement. The shape of this part of the spermatozoon has never been so clearly seen before. The crater-like notch on the vertex of the head may very well be some form of suction apparatus to facilitate the penetration of the ovum. With motion pictures we have seen how the

Fig. 2.—Head of human spermatozoon. The original from which this illustration was reproduced was magnified 27,000 diameters.

head of the spermatozoon penetrates the ovum as the first stage of fertilization. This is the first time such a definite irregularity in the structure of the head of the spermatozoa has been seen. As research in these higher magnifications goes on, we may have to throw overboard the old theories of chemotaxis and revamp much of what was heretofore believed true.

COMMENT

1. The belief that a spirem formation existed in the body of the human spermatozoon is not confirmed in this examination.

2. The old conception of the neck must now be changed. We are forced to call the neck the body of the spermatozoon, which appears as a highly complex and segmented structure.

3. There appears to be a heretofore undiscovered but definite irregularity at the vertex of the head of the spermatozoon which may be a distinct organ, such as a suction apparatus.

4. The tail is apparently a great deal longer than has been previously supposed, and it contains variations in structure which may be functional in character.

5. It is possible that the penetration of the spermatozoon into the ovum is effected by means of a specialized apparatus situated at the vertex of the head of the human spermatozoon.

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Special Articles

LEGAL RESPONSIBILITY FOR MEDICAL MALPRACTICE

III. FORGOTTEN ANCESTORS OF THE AMERICAN LAW OF MEDICAL MALPRACTICE

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This is the third of a series of six articles on "Legal Responsibility for Medical Malpractice." The two previous articles were published in The Journal March 8 and May 10, respectively.

In *Hodgson* v. *Bigelow*, 1939 (7 Atl. [2d] 338), the Supreme Court of Pennsylvania held that a physician's failure to give tetanus antitoxin for a "puncture" wound may constitute civil malpractice. In tracing the genealogy of this important American decision I found its early ancestors to be of English blood.

In the year 1553, Anthony Fitzherbert [1] published his "Natura Brevium," in which is contained the first intimation of the novel principle that one may become liable to another for negligent conduct which constitutes no breach of contract. This augury of a new basis in English law for fixing liability on careless conduct not only presaged the monumental development of tort law, which rose to a position of legal preeminence with the advent of the industrial revolution; it pointed out the way for modern doctrines of medical responsibility. One finds that the following passage which is quoted recurs in the arguments of counsel in English malpractice cases. One finds it alluded to in American decisions as well, even as late as the opinion of the Supreme Court of Pennsylvania in 1853 in the case of *McCandless* v. *McWha* (22 Pa. 261). Singularly, it deals not with the action of a physician but with the careless conduct of a blacksmith. The "Writ de Trespass sur le Case" [2] reads:

> But if a smith prick my horse with a nail, I shall have my action upon the case against him, without any warranty by the smith to do it well; and the writ shall be, wherefore he fixed a certain nail in the foot of a certain horse of J. at N. by which it became corrupted, so that the same horse for a long time could not labour, and he the said J. during that time lost the profit of his horse aforesaid, to the damage etc. For it is the duty of every artificer to exercise his art rightly and truly as he ought.[3]

In 1615, there came before the remarkable Sir Edward Coke, "father of the common law," at the time

1. La nouvelle Natura brevium du Iudge tresreverend Monsieur Anthoine Fitzherbert, London, Richard Totell, 1553.

In the preface Fitzherbert said: "In every Art and Science there are certain rules and foundations to which a man ought to give credit, and which he cannot deny.

"In like manner there are divers maxims and fundamentals in the knowledge of the common laws of the land, which a man ought for to believe very necessary for those who will understand the same law, especially at the beginning of their studies; for upon those fundamentals the whole law doth depend."

Any earlier pertinent materials of the common law are embalmed in the court French of the Year Books. Because of doubts as to the accuracy with which these precedents were recorded and their inaccessibility, English courts and counsel have let them lie there, with only occasional erudite allusions to the Abridgements.

2. Ibid., p. 214, D.

3. "If one retains counsel, and gives him his fee to assist him in the purchase of such a manor, if he becomes counsel for another, or discovers his counsel, case lies; yet though he warrants his client that he shall have the manor, but fails therein, yet if he does his endeavor, case does not lie; for perhaps he could not have the manor, i. e., it was impossible." (11 Henry VI, 24.55.)

chief justice of the Court of King's Bench, the case of *Everard* v. *Hopkins*,[4] from which comes the following passage:

In a special action upon the Case, the plaintiff in his declaration shews, that the defendant being a common Chyrurgeon, had undertaken the cure of his servant, being hurt with a cart-wheel; he shews farther, that he was not only careless of the cure (he being by promise and agreement between them, to have 5 Marks for the same cure) but he had also applied unwholesome Medicines, and with them had put him to more pain, per quod servitium suum amisit, per spatium of one whole year; unde actio.

Coke, Chief Justice said:

It is also here laid, that he did apply, indebita and insalubria Medicina; for this the master may have an action clearly; but the servant cannot have an action upon this agreement, but he may have an action upon the case for his applying of unwholesome medicines to him. It is considerable, whether the master here may have an Action upon the Case, upon an Action upon the Case, this he may have, if the master sends his servant to pay money for him upon the penalty of a bond! and in his way a smith, in shoeing, doth prick his horse, and so by reason of this the money is not paid; this being the servant's horse, he shall have an action upon the case for the special wrong which he had sustained by this, by the non-payment of his money, occasioned by this. . . .

Observe that the ratio decidendi of the case is that a master who has contracted with a physician may recover damages for negligent administration of medicine to his servant. Remarks as to the servant's right of action were unessential to the decision and so constitute mere dictum. Sometimes, however, the dictum of today becomes the law of tomorrow. Such was this case; the dictum that the servant, though a stranger to the contract of employment, had an independent action against the derelict physician on the ground of negligence became law by force of later cases (*Pippin* v. *Sheppard*, 11 Price 400; *Gladwell* v. *Steggall*, 8 Scott, 60; 5 Bing. N.C. 733; *Longmeid* v. *Holliday* [Court of Exchequer 1851] 6 Exch. 761 [dictum]).

There is current in some quarters a false notion that only the "quack" need be concerned with mala praxis. How unsubstantial this belief is can nowhere be better illustrated than in the celebrated English case of *Slater* v. *Baker and Stapleton* (Common Bench), Michaelmas Term, 8 Geo. III, 1767, 2 Wilson 359. This was a special action on the case against a surgeon and an apothecary for unskilfully disuniting the callus of the plaintiff's leg after it was set.

The facts were these. Slater broke both bones of one leg. A local surgeon set them and attended the patient for nine weeks. By the end of four weeks, callus had formed, and soon after the injured man was beginning to walk a bit with crutches. But a protuberance had arisen, and Slater called in Stapleton, a local apothecary, to remove the bandage from his leg. Stapleton declined to do it himself and prevailed on Slater to call into conference defendant Baker, for twenty years first surgeon of St. Bartholomew's Hospital in London. Evidently Baker was not satisfied with the result, for on his third visit he brought with him a new contrivance of his invention for extending the leg, which he applied without obtaining Slater's consent to its use or to the breaking of the callus and resetting of the bones. One reads:

The defendants came to the plaintiff, Baker took up the plaintiff's foot in both his hands and nodded to Stapleton, and then Stapleton took the plaintiff's leg upon his knee, and the leg gave a crack, when the plaintiff cried out to them and said "you have broke what nature had formed;" Baker then said to the plaintiff, "You must go through the operation of extension," and Stapleton said, "we have consulted and done for the best."

The leg did not reunite as anticipated, and the plaintiff, who was left with a poorer result, sued both Stapleton and Baker.

Other surgeons called as witnesses testified variously that to disunite the callus was not customary except when the leg as set was very crooked; that the way of making it straight was by compression and not by extension. They had not the least idea of the instrument spoken of for extension. Some said they would not have disunited a hard callus even on the patient's request and that in no case would they do so without his consent. All agreed that Baker was eminent in his profession. One reads further:

A woman called as a witness swore, that when the plaintiff came home he could walk with crutches; that the defendant Baker put on to the plaintiff's leg an heavy steel thing that had teeth, and would stretch or lengthen the leg; that the defendants broke the leg again, and three or four months afterwards the plaintiff was still very ill and bad of it.

The jury awarded a verdict of £500 against the defendants jointly.

The defendants moved that the verdict ought to be set aside; a part of their contention read:

Baker has been above 20 years the first surgeon in St. Bartholomew's Hospital, reads lectures in surgery and anatomy, and is celebrated for his knowledge in his profession as well as his humanity; and to charge such a man with ignorance and unskilfulness upon the records of this court is most dreadful. All the witnesses agreed Mr. Baker does not want knowledge, therefore this verdict ought not to stand.

The whole court, in an opinion upholding the verdict and affirming the judgment, said:

When we consider the good character of Baker, we cannot well conceive why he acted in the manner he did; but many men very skilful in their profession have frequently acted out of the common way for the sake of trying experiments. Several of the witnesses proved that the callus was formed and that it was proper to remove plaintiff home; that he was free from pain and able to walk with crutches. We cannot conceive what the nature of the instrument made use of is: Why did Baker put it on, when he said the plaintiff had fallen into good hands, and when plaintiff only sent for him to take off the bandage? It seems as if Mr. Baker wanted to try an experiment with this new instrument.

2dly, It is objected, that this is not the proper action, and that it ought to have been trespass vi et armis.[5]

In answer to this, it appears from the evidence of the surgeons that it was improper to disunite the callus without consent; this is the usage and law of surgeons: then it was ignorance and unskilfulness in that very particular, to do contrary to the rule of the profession, what no surgeon ought to have done; and indeed it is reasonable that a patient should be told what is about to be done to him, that he may take courage and put himself in such a situation as to enable him to undergo the operation. . . . For anything that appears to the court, this was the first experiment made with this new instrument; and if it was, it was a rash action, and he who acts rashly acts ignorantly: and although the defendants

4. *Everard* v. *Hopkins* (Court of Kings Bench) 1615, 2 Bulst. 332; 1 Roll. Rep. 124; 80 E. R. 1164.

5. The plaintiff had a clearcut cause of action for the battery arising from the breaking of his leg, to which he had not given his consent, and for this immediate, intended contact trespass vi et armis was the appropriate action. To support it the plaintiff would not need to prove negligence but only lack of consent and consequent injury.

But in this instance plaintiff sued in "case," and to support this form of action he needed to prove negligence; so the court was confronted with the interesting question: Can an intentional, unauthorized act toward a patient sufficient to constitute "battery" at the same time constitute "negligence"? The answer is yes when the omitted consent is to an experimental treatment attended with risk of failure and is therefore, in the view of the medical profession, improper to apply without prior consultation of the patient.

Today in such cases the plaintiff usually proceeds on the theory of battery, because of the fewer elements required to make proof.

in general may be as skilful in their respective professions as any two gentlemen in England, yet the court cannot help saying, that in this particular case they have acted ignorantly and unskilfully, contrary to the known rule and usage of surgeons.

This case illustrates several interesting points:

1. The eminence of the practitioner and the purity or benevolence of his motive afford no defense to a civil action for malpractice. This follows because the object of the action is not punishment of the physician for moral turpitude but compensation for an injury caused by medical dereliction. The actionable violation of the patient's right of personal integrity may consist of either intentional or negligent conduct.

2. One who collaborates, even in a minor role, in the culpable act, as did Stapleton in holding the leg, becomes equally liable in damages as a "joint tort feasor." Pending opportunity to give deserved comprehensive attention to the important question of joint responsibility in medical transactions, the general rule may be stated thus: It is possible for two physicians to be called in to treat the same patient concurrently and yet for neither to be liable for the lack of skill or the negligence of the other. They have a right to make such division of the medical service to be rendered as, in their sound judgment, circumstances require. In such case each, in serving with the other, is held answerable for his own medical conduct and for all wrongful acts or omissions of the other that he observes and permits to continue without protest or which, using reasonable diligence, he should have noticed; but this, in main, is the limit of his liability (*Morey* v. *Thybo*, 199 Fed. 760,118 C.C.A. 198, 42 L.R.A. [N.S.] 785).

3. Though one might suppose that by submitting himself to treatment a patient thereby impliedly consents to any procedure which the physician deems appropriate and administers in good faith, this assumption is too broad. In respect to unusual procedures the physician should disclose his intention and preferably put before the patient the alternatives, the intended purpose and a fair statement of the risk, all with a view to enabling the patient to make a fair choice and to give his actual consent.[6] It may be well to bear in mind two types of cases: (1) those in which a physician wishes to try a novel or experimental remedy not yet applied as a medical measure to the treatment of human beings, even though its value has been demonstrated by animal experimentation and laboratory tests and even though in the opinion of the user it is intrinsically sound, and (2) all cases in which some procedure is proposed which is calculated to effect radical alteration of the status quo, with an element of appreciable risk, such as certain operations or the administration of drugs involving a substantial hazard of tissue damage or of profound constitutional reactions. The latter cases are not so clearcut as those in group 1, but they demand thought as to whether bare consent of the patient is enough to warrant going ahead with the procedure. In *Theodore* v. *Ellis* (Supreme Court of Louisiana, 1917) 75 So. 655, it was held that a first drainage operation for a disorder of the bladder was warranted under a broad consent from the patient but that subsequent lobectomy of the prostate gland, when the surgeon had not made a full disclosure of the nature of the operation and its purpose, was not.

This obligation of disclosure has a reasonable basis in fair play toward the patient. But it rests even more solidly on the duty of disclosure springing (1) from the relationship of trust and confidence between physician and patient, which partakes of a fiduciary character, and (2) from the obligation an expert may owe to a novice. Usually parties deal at arm's length, and neither owes the other the benefit of his superior knowledge ("caveat emptor"). But when one person is an expert in possession of technical information necessary to the enlightened decision of a novice who justifiably relies on him for guidance, a duty to disclose material facts may arise. The case is even stronger in regard to the physician, for it may be argued that his very employment is in part as a counsellor on health. An interesting analogy exists in the law of trusts. If A conveys property to B, as trustee, for the use and benefit of C, a trust is created. B, for purposes of administering the property, has the full authority incident to possession of the legal title (similar to that of a physician whose general control is authoritative in managing the health of the sick patient). The trustee can negotiate ordinary transactions in the interest of the trust without consulting C, the beneficiary, who holds the equitable title. But if he proposes any unusual investment or any action which may threaten dissipation of the corpus (principal or "body" of the trust), he must make a full disclosure to the beneficiary and obtain his informed consent before he takes such action. Otherwise he is responsible for consequent injury.

4. *Slater* v. *Baker* shows that what is "due care" and what is negligence in medical practice is a question of fact, determinable by the jury in each new case. The jury is to be guided by the testimony of expert witnesses as to what the average practitioner at the time and the place of the conduct would consider prudent or bad practice.

5. Lastly, it stands for the now well established principle that when the plaintiff's action is based on the defendant's failure to use due skill in a particular transaction, evidence as to the skill the defendant used in treating other patients is not admissible.[7]

A case which has been much more cited both in America and in England than its intrinsic value merits is that of *Seare* v. *Prentice*, decided in 1807 by Lord Ellenborough, then chief justice of the King's Bench [8] (8 East, 347; 103 E.R. 376). Seare, a shoemaker, brought an action on the case against the defendant, Prentice, whom he had employed as a surgeon, for negligently, ignorantly and unskilfully reducing his dislocated elbow and fractured arm. At the trial, Justice

6. Substantial reasons may legally justify nonobservance of the normal duty to disclose. For instance, suppose a person is so ill that his life can be saved only by a drug the administration of which is itself attended by some risk, such as sulfanilamide for a patient with streptococcic septicemia due to otitis media. The patient is of nervous temperament or so prostrate that disclosure of the danger might precipitate a fatal crisis. The drug may be administered without disclosure of the risk involved.

7. Results of similar treatment of other patients has probative value and is admissible when defendant's professional capacity is put in issue or a claim is made that the very method of treatment itself was medically improper.

8. It was he who decided the remarkable case of *Ashford* v. *Thornton*, 1 Barn. and Ald. 405, (1818). Richard Thornton, on jury trial at Warwick, was found "not guilty" of the murder of Mary Ashford, whereupon her brother, William Ashford, sued out an appeal of murder against him. Appellee Thornton, when he was brought into the Court of King's Bench, pleaded viva voce: "Not guilty, and I am ready to defend the same by my body," and taking a gauntlet from his right hand, he threw it on the floor. Judge Ellenborough reviewed the ancient common law precedents and was forced to conclude that no change had been made in the almost forgotten rule that "the mode of trial by law in such a case of appeal is by 'battle,' at the election of the appellee except where the appellee is an infant or a woman or above sixty years of age." He declared: "The law of the land is in favour of the trial by battle, and it is our duty to pronounce the law as it is, and not as we may wish it to be." There was great excitement at this prospect of a trial by combat, and the public expected to see the battle fought out before the judges at Tothill Fields; but Ashford, being more resolving in the law than in the lists, refused to proceed further, and the appeal was dismissed. The case occasioned a sensation and resulted in the statute of 59 Geo. III C. 46, which abolished criminal appeals and trials by battle in writs of right.

Heath instructed the jury that unless negligence was proved they could not investigate the want of skill. Since the evidence did not substantiate negligence, a verdict was brought in for the defendant, under direction of the judge. In reviewing the proceedings, Lord Ellenborough found that the defendant was entitled to a verdict because "no want of skill was imputed to the defendant," but he condemned the dictum of the trial court that unless negligence was proved the jury could not investigate the want of skill. Since, as he confessed, the question did not arise on the evidence, it follows that Ellenborough's own remarks on the subject are themselves mere dictum, because unnecessary to a decision of the case, but they have been cited often. One reads:

> . . . an ordinary degree of skill is necessary for a surgeon who undertakes to perform surgical operations; which is proved by the case of Wilson, and indeed by all analogous authorities; in the same manner as it is necessary for every other man to have it in the course of his employment; as the farrier who undertakes to cure my horse must have common skill at least in his business, and that is implied in his undertaking: and although I am ready to admit that a surgeon would be liable for crassa ignorantia, and would be justly responsible in damages for having rashly adventured upon the exercise of a profession, without the ordinary qualification of skill, to the injury of a patient: yet the question did not arise upon the evidence in this case; for no want of skill was imputed to the defendant: and therefore the opinion of the learned Judge upon that point does not affect the merits of the verdict upon the evidence in the case.

English lawyers sometimes assert that this case was the first to lay down the rule that a physician must use skill as well as care. I have shown, however, that "unskilfulness" was made the basis of decision in the earlier English case of *Slater* v. *Baker and Stapleton* (1767) and was recognized as far back as Roman law.[9]

Many courts, today, speak of negligence and failure to use due skill as separate legal entities. Actually, they can mean by so doing only to break down negligent conduct of a medical case into causal components. The various deficiencies which may result in a negligent performance may be represented as follows:

1. X is ignorant, lacking in education or specific information necessary for the particular undertaking.

Example.—X, who has operated only on the abdomen and never familiarized himself with surgical procedures on the brain, in a nonemergency in a city where competent brain surgeons are available essays a difficult operation on the brain. He is unable to complete it successfully because of failure to foresee the necessity for certain special instruments and precautions.

Though he uses all the care and skill he has, the very assumption, unnecessarily, of an undertaking beyond his preparation is negligent and permeates the entire conduct of the case.

But note: the law is interested in his incapacity primarily because of the injury done to the patient through the resulting inability to conduct the case properly. If the same surgeon, despite his poor qualification, completes the operation successfully, his undertaking the task still remains "negligent" by common usage but not in law, because the treatment itself, the actual conduct of the case, is free from fault. The physician has acted at his peril, but the ominous dangers threatened by his rash assumption to act have not materialized.

2. X is well informed as to theory but lacks in requisite experience and so in the skill demanded by the undertaking.

Example: A recently graduated medical student who has not taken a surgical internship or had actual experience is profoundly versed in the literature on surgical operations on the brain. He essays a (nonemergency) operation on the brain, believing he can duplicate one of the operations which he has seen Dr. Harvey Cushing do or one of which he has read descriptions. The operation fails for want of skill.

3. X has information and experience, but due to inaptitude he has never acquired the skill possessed by the "average practitioner" in his community.

Example: A practitioner of long standing fails to reduce and set a Colles fracture with the skill which the average practitioner would employ. Marked deformity results.

4. X has information, experience and skill but fails to apply skill to the particular case, with consequent injury.

Example: X knows that aminopyrine is a dangerous drug but prescribes it freely for persistent headache without making periodic studies of the blood or carefully checking the clinical response. Full-blown granulocytopenia develops in the patient.

5. X has information, experience and skill but in a transaction not requiring skill fails to use such care or diligence as the average practitioner would apply.

Example: X abandons the care of a patient with a simple ailment without legally terminating the relationship of physician and patient. In consequence, a preventable complication develops which the average practitioner in attendance could have prevented.

6. X has knowledge, judgment, care and skill but fails to apply average judgment to the transaction.

Example: A child under 2 years of age is admitted to a hospital with osteomyelitis and shows evidences of acute infection and septicemia, profound dehydration and shock; the surgeon performs an immediate, radical surgical operation, which precipitates death. In the face of contraindications which would invariably deter the average surgeon, precipitate action without clinical basis may involve negligence, however carefully and skilfully the operation is performed. In this case the basis is failure to exercise average judgment.

7. X has knowledge, judgment, care and skill but fails to maintain control of the medical transaction; or he entrusts properly delegable functions to one he reasonably should have known to be incompetent.

Example: X, in carrying out an abdominal operation, relies on "green" nurses, pressed into emergency service, to make the count of the sponges used, without personally verifying its accuracy. A retained sponge causes tissue necrosis.

Example: While conducting a vitally important investigation of a patient's renal function, X delegates the laboratory work to Y, an independent laboratory technician (an independent contractor), whose results have several times been found undependable. Y negligently arrives at erroneous conclusions. As the result of the normal reports, the patient is subjected to a contraindicated operation. X had reasonable notice of Y's incompetence; it was therefore negligent to entrust the investigations to her or, in the alternative, to accept her results without verification.

Note: 1. In all of these instances, the dereliction may lie either in an affirmative act (misfeasance) or

9. Smith, H. W.: Legal Responsibility for Medical Malpractice: I. The Legal Matrix of Medical Malpractice, J. A. M. A. **116:** 942 (March 8) 1941.

in an omission to act when there is a duty to do so (nonfeasance). In the presence of a physician-patient relationship, whether the omitted action is negligent depends on whether a prudent physician would have considered neglect to do the omitted thing as bad practice. The mere fact that he himself, in like circumstances, would have done the omitted thing is not enough: he might have considered it wise through an abundance of caution, while current practice would not have considered the omission as culpable.

2. In each case, the standard of knowledge, judgment, care or skill which the practitioner must bring to bear is that which the average practitioner of his own class and community would apply under similar circumstances.

3. There may be combinations of two or more of these seven causes of negligent conduct of a case.

One of the most influential statements of principle in respect to the law of malpractice occurred in the charge to the jury given by Tindal, chief justice, in the English case of *Lanphier and Wife* v. *Phipos* (cases at nisi prius), 1838, 8 Carrington & Payne, 475.

The facts were these. Mrs. Lanphier, in September 1835, while traversing a field became alarmed at the spectacle of an approaching cow, gave a sudden turn, tripped and fell on the wrist of her right hand, causing "a fracture of the small bone of the arm, and a partial dislocation of the third bone of the palm of the hand." The defendant was called and arrived within an hour after the fall. A neighbor, testifying for the plaintiff, declared she expressed the opinion to the physician that the wrist was injured but that he took hold of the patient's hand and then gave a contrary opinion. He said the injury was not in the wrist but in the arm, put splints on and bound it from below the elbow to the wrist, leaving the hand hanging down. Swelling gradually increased, and vinegar was applied by the defendant's direction, and he expressed his opinion that "it was doing very well." The witness drew his attention to the increase of swelling and inflammation, and he removed the splints and examined the arm; whenever she spoke to him on the subject, he expressed the opinion that it was doing very well. The splints were kept on for about seven weeks. The inflammation spread to the shoulder, and the husband was alarmed and complained, so the defendant sent some kind of oil to bathe it. The witness told him that if it were hers (Mrs. Jones's) she would not be satisfied with the way in which it was progressing; but he still said he thought it was doing very well. When the defendant had attended the patient about seven weeks, she retained a new surgeon, V. He applied longer splints, which supported the hand, and instituted special treatment to reduce the inflammation; but despite improvement, the patient lost the use of her hand, so that she could not use a knife or fork or dress or undress herself with it.

On these facts, at the trial, Mr. Calloway, of Guy's Hospital, and Mr. Tyrrell, of St. Thomas's Hospital, were allowed to give their opinions.

Both considered that defendant's treatment of the case was injudicious, particularly in suffering the hand to hang down, and in not making sufficient efforts, by lotions and other means, to reduce and keep down the inflammation.

For defendant, Mr. Luke of the London Hospital, who examined the injury in June 1937, under a judge's order, testified that in his opinion there had not been any mismanagement on the part of the defendant and that such was the opinion of the second surgeon, V. Three other surgeons, after hearing Mr. Luke's evidence of what he discovered and ascertained on the examination, expressed it as their opinion that the defendant was not at all to blame.

Tindal, chief justice, in summing up, after stating the pleadings, charged the jury as follows:

What you will have to say is this, whether you are satisfied that the injury sustained is attributable to the want of a reasonable and proper degree of care and skill in the defendant's treatment. Every person who enters into a learned profession undertakes to bring to the exercise of it a reasonable degree of care and skill. He does not undertake, if he is an attorney, that at all events you shall gain your case, nor does a surgeon undertake that he will perform a cure; nor does he undertake to use the highest possible degree of skill. There may be persons who have higher education and greater advantages than he has, but he undertakes to bring a fair, reasonable, and competent degree of skill, and you will say whether, in this case, the injury was occasioned by the want of such skill in the defendant. The question is, whether this injury must be referred to the want of a proper degree of skill and care in the defendant or not. The action is not brought for any injury sustained by the husband, but it is brought by the wife for the injury which she has sustained by the loss of the use of her hand. The husband must be joined in the action, but the damages are to be given for the injury sustained by her. His Lordship then read and commented on the evidence, and then left the case to the jury, who found a verdict for the plaintiff. Damages £100.

In surveying English common law, one feels constrained to see what Blackstone said on the subject. In his "Commentaries on the Laws of England" [10] is this passage:

4. Injuries affecting a man's health are where, by any unwholesome practices of another, a man sustains any apparent damage in his vigour or constitution. As by selling him bad provisions, or wine; by the exercise of a noisome trade, which infects the air in his neighborhood; or by the neglect or unskilful management of his physician, surgeon, or apothecary. For it hath been solemnly resolved, that mala praxis is a great misdemeanour and offence at common law, whether it be for curiosity and experiment, or by neglect; because it breaks the trust which the party has placed in his physician, and tends to the patient's destruction.

The learned Blackstone stated the rule correctly but erred as to its reasons. He said the physician's dereliction is a misdemeanor, resting on a "breach of trust." I have shown, on the contrary, that the usual basis is civil and that at common law medical responsibility springs partly from "contract" (an implied warranty by the physician in accepting employment that he possesses average qualifications) and partly from "tort" (especially doctrines of negligence). Both of these bases of liability rest on principles of compensation for injury rather than of punishment for a delict. Later it will be seen that of these two the "tort" basis is of greater importance. A neighboring passage suggests that Blackstone fell into error because he was thinking of the Roman law.

The precedents which have just been surveyed have a peculiar interest as the earliest "blood ancestors" of the present law of malpractice both in England and in the United States. Their intrinsic worth also warrants attention, for their doctrines are still law. They have been added to and elaborated by the later cases but not overturned. They have been left behind, but they still point the direction in which the law is traveling.

10. Blackstone, William: Of Wrongs and Their Remedies, Respecting the Rights of Persons, in Private Wrongs, in Commentaries on the Laws of England, Oxford, 1769, book 4, chap. 8, p. 122.

GLANDULAR PHYSIOLOGY AND THERAPY

ADRENAL CORTEX INSUFFICIENCY

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This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.—ED.

CLINICAL PICTURE OF ADRENAL CORTEX INSUFFICIENCY

The syndrome of adrenal cortex insufficiency was first described by Thomas Addison, in his classic treatise, published in 1855. This symptom complex as observed in Addison's disease is characterized by an insidious onset and progressive development of fatigability and asthenia to the point of utter exhaustion, associated with varying degrees of anorexia, nausea and vomiting. Very occasionally diarrhea and abdominal pain are present. The symptoms may appear in the course of weeks, months or even years. At times, however, the tempo of the disease may be greatly accelerated. This may occur either spontaneously or in response to a withdrawal of sodium salts from the diet, or in association with an acute infection, and may, in the course of a few days, terminate fatally. These abrupt episodes of adrenal insufficiency are termed "crises." In a few instances the symptoms and signs of hypoglycemia may dominate the clinical picture, particularly among patients receiving salt or desoxycorticosterone acetate therapy.

Pigmentation and arterial hypotension are the physical signs usually exhibited by patients with adrenal cortex insufficiency. The pigmentation is brownish and may be either diffuse or blotchy in distribution. It is most typically observed in the mucous membranes of the buccal cavity. However, there are patients in whom no pigmentation develops. Hypotension is almost invariably present among patients seeking medical aid, but under emotional stress the blood pressure may momentarily rise to normal or even to abnormal levels. During crises it falls to strikingly low levels, and the patient presents a picture of dehydration and shock.

PATHOLOGIC PHYSIOLOGY

In the past decade great advances have been made in the clarification of certain mechanisms involved in the development of adrenal cortex insufficiency. These have been discussed extensively elsewhere in this series, but, since they constitute the basis of present therapy, it is essential that those with clinical significance be considered briefly at this point.

Salt and Water Metabolism.—In 1927 Baumann and Kurland [1] and Marine and Baumann [2] showed that the sodium concentration in the blood of adrenalectomized cats was decreased and that a solution of sodium chloride prolonged life more effectively than did solutions of other electrolytes or of dextrose. In 1932 and 1933 it was shown by the writer [3] that the concentration of sodium in the blood of patients suffering from uncompensated adrenal cortex insufficiency was decreased and that replacement of the sodium ion relieved this condition. It was also shown that withdrawal of the sodium ion from the diet of patients with Addison's disease precipitated acute adrenal cortex insufficiency.[4] It was then observed in dogs that the loss of sodium following adrenalectomy results from increased excretion of sodium ions by the kidney.[5] These observations have been amply confirmed,[6] and Harrop and associates [7] and Allers [8] independently pointed out that adrenalectomized dogs could be maintained in good health indefinitely if sodium salts were administered in sufficient amounts, particularly if the potassium content of the diet was reduced. A disturbance in water metabolism is intimately related to that of the concentration of sodium ions in adrenal cortex insufficiency. Thus, there is a tendency for water to be lost as the insufficiency progresses up to the point where a fall in blood pressure causes oliguria.[5] This is associated with a consistent decrease in plasma volume. However, water is not, as a rule, lost from the body as rapidly as is sodium. This is shown by the fact that the sodium concentration of the blood decreases. It has been shown that acute adrenal cortex insufficiency may be induced in a patient with Addison's disease by restricting the intake of fluid, despite the administration of salt. Under these conditions a crisis associated with a fall in blood pressure, collapse and a decrease in plasma volume without a decrease in blood sodium appeared in a patient studied by Willson and Sunderman.[9] A loss of sodium without a decrease in plasma volume, i. e., without a simultaneous loss of water, does not regularly give rise to the picture of adrenal cortex insufficiency.

Potassium Metabolism.—An increase in the concentration of the potassium ion was first observed in animals by Baumann and Kurland,[1] in 1927, and in human subjects with adrenal insufficiency by the writer in 1932.[3] This disturbance is closely related to disturbances in sodium and water metabolism. In general, as sodium is lost from the body, potassium in the blood serum tends to increase and the ability of the body to excrete potassium ions is impaired. Kendall and associates [10] and Zwemer and Truszkowski [11] empha-

From the Departments of Medicine and Neurology, College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital and Neurological Institute.

1. Baumann, E. J., and Kurland, S.: Changes in the Inorganic Constituents of Blood in Suprarenalectomized Cats and Rabbits, J. Biol. Chem. **71**: 281 (Jan.) 1927.

2. Marine, David, and Baumann, E. J.: Duration of Life After Suprarenalectomy in Cats and Attempts to Prolong It by Injections of Solutions Containing Sodium Salts, Glucose and Glycerol, Am. J. Physiol. **81**: 86 (June) 1927.

3. (a) Loeb, R. F.: Chemical Changes in the Blood in Addison's Disease, Science **76**: 420 (Nov. 4) 1932; (b) Effect of Sodium Chloride in Treatment of a Patient with Addison's Disease, Proc. Soc. Exper. Biol. & Med. **30**: 808 (March) 1933.

4. (a) Harrop, G. A.; Weinstein, Albert; Soffer, L. J., and Trescher, J. H.: The Diagnosis and Treatment of Addison's Disease, J. A. M. A. **100**: 1850 (June 10) 1933. (b) Harrop, G. A.: Diagnosis and Treatment of Addison's Disease, ibid. **101**: 388 (July 29) 1933. Loeb.[3b]

5. Loeb, R. F.; Atchley, D. W.; Benedict, Ethel M., and Leland, Jessica: Electrolyte Balance Studies in Adrenalectomized Dogs with Particular Reference to the Excretion of Sodium, J. Exper. Med. **57**: 775 (May) 1933.

6. Harrop, G. A.; Soffer, L. J.; Ellsworth, Read, and Trescher, J. H.: Studies on Suprarenal Cortex: III. Plasma Electrolytes and Electrolyte Excretion During Suprarenal Insufficiency in the Dog, J. Exper. Med. **58**: 17 (July) 1933. Harrop and others.[4]

7. Harrop, G. A.; Soffer, L. J.; Richardson, W. N., and Strauss, Margaret: Studies on the Suprarenal Cortex: IV. The Effect of Sodium Salts in Sustaining the Suprarenalectomized Dog, J. Exper. Med. **61**: 839 (June) 1935.

8. Allers, W. D.: Influence of Diet and Mineral Metabolism on Dogs After Suprarenalectomy, Proc. Staff Meet., Mayo Clin. **10**: 406 (June 26) 1935.

9. Willson, D. M., and Sunderman, F. W.: Studies in Serum Electrolytes: The Effect of Water Restriction in a Patient with Addison's Disease Receiving Sodium Chloride, J. Clin. Investigation **18**: 35 (Jan.) 1939.

10. Allers, W. D.; Nilson, H. W., and Kendall, E. C.: Studies on Adrenalectomized Dogs: The Toxic Action of Potassium, Proc. Staff Meet., Mayo Clin. **11**: 283 (April 29) 1936.

11. Zwemer, R. L., and Truszkowski, R.: Potassium: A Basal Factor in the Syndrome of Cortico-Adrenal Insufficiency, Science **83**: 558 (June 5) 1936.

sized the susceptibility of adrenalectomized animals to the injection or ingestion of potassium salts. Wilder and his collaborators [12] emphasized the danger attendant on the ingestion of large amounts of potassium salts by patients with Addison's disease. Despite the deleterious effects of the potassium ion in adrenal cortex insufficiency, the concept that death from this insufficiency results from potassium poisoning is untenable.

Renal Function.—Marshall and Davis [13] were the first to point out, in 1916, an increase in nonprotein nitrogen in the blood of adrenalectomized animals. In patients with adrenal cortex insufficiency an increase in nonprotein nitrogen, inorganic phosphorus and sulfate may occur. Furthermore, decreases in urea clearance may be present even in the absence of nitrogen retention. These disturbances have been shown by Stahl, Kuhlmann and Urban [14] to be associated with hemoconcentration and presumably with a decrease in renal blood flow. Observations on creatinine clearance in adrenal cortex insufficiency by Margitay-Becht and Gömöri [15] led to the same inference. The disturbances in electrolyte and water metabolism already discussed are to a large extent referable to a derangement of normal renal activity [16] other than that resulting in decreased renal blood flow. It seems probable that this derangement is related to tubular reabsorption.

Carbohydrate Metabolism.—Porges,[17] in 1909, was the first to report the presence of hypoglycemia in patients suffering from Addison's disease and in adrenalectomized animals. In recent years the studies of Britton and Silvette,[18] Long and his colleagues [19] and Kendall and his associates [20] have shown that a decrease in glycogen storage in the liver and in sensitivity to insulin are also characteristic of adrenal cortex insufficiency.[21] The disturbances in carbohydrate metabolism vary considerably in different species, and they vary greatly in intensity in persons with Addison's disease, but they may be of sufficient gravity to prove fatal. It is generally believed that the abnormalities of carbohydrate metabolism result from a decrease in the utilization of carbohydrate and a decrease in gluconeogenesis.[22] The disturbances in carbohydrate metabolism as seen in Addison's disease vary independently of the disturbances in salt and water metabolism.[23] It has been amply established by the work of Long and associates,[19] Thorn,[24] Kendall [20a] and our own laboratory [25] that various steroids isolated from the adrenal cortex exhibit striking differences in their effect on carbohydrate and electrolyte metabolism.

Nitrogen Metabolism.—Nitrogen retention and a decrease in the excretion of ammonia appear in the development of severe adrenal cortex insufficiency and are probably in part due to decrease in renal blood flow. Following the administration of various extracts of adrenal cortex there is often a temporary increase in the urinary excretion of nitrogen perhaps due to improvement in renal function. On the other hand, it has been shown by Long and co-workers [19] and Kendall and his associates [20a, b] that the nitrogen excretion of diabetic rats or of fasting normal rats may be increased by the administration of certain adrenal steroids. This increase has been shown to be due to gluconeogenesis from body protein, which may be the primary effect, but which possibly arises in response to a decrease in the utilization of carbohydrate.

Adynamia.—This manifestation of adrenal cortex insufficiency, which plays a major part in the subjective manifestations of Addison's disease, has been extensively studied by Ingle [26] in rats. From the results of his work it is certain that adynamia results chiefly from the disturbances in carbohydrate metabolism and to a lesser extent from the loss of salt and water and decrease in blood flow. Whether or not other factors play a part is not known.

Arterial Hypotension.—The fall in blood pressure to shock levels during crises of adrenal cortex insufficiency is dependent to a large extent on the disturbances in salt and water metabolism. The chronic but milder degrees of hypotension may also be dependent on the same abnormality, since the blood pressure may be raised by the administration of sodium salts as well as by the administration of desoxycorticosterone acetate, which primarily affects the metabolism of salt and water. Whether other factors contribute to hypotension is not known.

Miscellaneous Disturbances.—Among these, pigmentation occupies a prominent position. This abnormality, although not universally present in Addison's disease, is extremely common, yet its mechanism remains totally obscure. Sensitivity to change in temperature, particularly to cold, and sensitivity to pain stimuli, which are characteristics of patients and animals in adrenal cortex insufficiency, may possibly be correlated with the disturbances in carbohydrate and in electrolyte metabolism, as indicated by the studies of Kendall.[20a] The moderate lowering of the basal metabolic rate occasionally observed is probably on a similar complex basis. The mechanisms acting in the production of hypercalcemia, elevation of serum phosphatase, retention of bromsulphalein and gynecomastia, all of which are sometimes present in addisonian patients, are not known. Focal and diffuse neurologic disorders in adrenal cortex insufficiency result probably from hypoglycemia or from decreased cerebral blood flow or from both.

In 1933 Swingle and collaborators [27] suggested that a hormone of the adrenal cortex had an effect on the

12. Wilder, R. M.; Kendall, E. C.; Snell, A. M.; Kepler, E. J.; Rynearson, E. H., and Adams, Mildred: Intake of Potassium: An Important Consideration in Addison's Disease: A Metabolic Study, Arch. Int. Med. **59**: 367 (March) 1937.

13. Marshall, E. K., Jr., and Davis, D. M.: The Influence of the Adrenals on the Kidneys, J. Pharmacol. & Exper. Therap. **8**: 525 (Sept.) 1916.

14. Stahl, Jules; Kuhlmann, D., and Urban, M.: A propos du mécanisme de l'insuffisance rénale au cours de l'insuffisance surrénalienne expérimentale, Compt. rend. Soc. de biol. **127**: 1286, 1938.

15. Margitay-Becht, A., and Gömöri, P.: Die Nierenfunktion bei der Addisonschen Krankheit, Ztschr. f. d. ges. exper. Med. **104**: 22, 1938.

16. Harrison, H. E., and Darrow, D. C.: Renal Function in Experimental Adrenal Insufficiency, J. Clin. Investigation **17**: 503 (July) 1938.

17. Porges, O.: Ueber Hypoglykämie bei Morbus Addison sowie bei nebennierenlosen Hunden, Ztschr. f. klin. Med. **69**: 341, 1909-1910.

18. Britton, S. W., and Silvette, Herbert: The Apparent Prepotent Function of the Adrenal Glands, Am. J. Physiol. **100**: 701 (May) 1932.

19. Long, C. N. H.; Katzin, B., and Fry, E. G.: The Adrenal Cortex and Carbohydrate Metabolism, Endocrinology **26**: 309 (Feb.) 1940.

20. (a) Kendall, E. C.: The Function of the Adrenal Cortex, Proc. Staff Meet., Mayo Clin. **15**: 297 (May 8) 1940. (b) Sprague, R. G.: The Influence of Extract of the Adrenal Cortex on Glycogenesis in Fasting Rats, Proc. Staff Meet., Mayo Clin. **15**: 291 (May 8) 1940. (c) Wells, B. B.: The Influence of Crystalline Compounds Separated from the Adrenal Cortex on Gluconeogenesis, Proc. Staff Meet., Mayo Clin. **15**: 294 (May 8) 1940.

21. This view of an intimate relation between carbohydrate metabolism and the function of the adrenal cortex has been amply confirmed and is contrary to that expressed by the writer in the first edition of this book.

22. Long and others.[19] Kendall and others.[20]

23. Loeb, R. F.; Atchley, D. W., and Parson, William: The Significance of Certain Chemical Abnormalities Found in the Blood in Addison's Disease, Tr. A. Am. Physicians **52**: 228, 1937.

24. Thorn, G. W.: Personal communication to the author.

25. Ferrebee, J. W.; Ragan, Charles; Atchley, D. W., and Loeb, R. F.: A Comparison of Certain Effects of Desoxycorticosterone Acetate, Corticosterone and Cortical Extract in a Patient with Addison's Disease, Endocrinology **27**: 360 (Sept.) 1940.

26. Ingle, D. J.: The Work Performance of Adrenalectomized Rats Treated with Corticosterone and Chemically Related Compounds, Endocrinology **26**: 472 (March) 1940.

27. Swingle, W. W.; Pfiffner, J. J.; Vars, H. M.; Bott, P. A., and Perkins, W. M.: The Function of the Adrenal Cortical Hormone and the Cause of Death from Adrenal Insufficiency, Science **77**: 58 (Jan. 13) 1933.

peripheral vascular bed. The evidence provided was not convincing. However, the fact that an extract of the adrenal cortex may effect prompt relief in dogs suffering from severe adrenal cortex insufficiency without causing demonstrable changes in the blood volume or the electrolyte pattern [28] suggests the possibility of action either on tissue of the nervous system or perhaps on the capillaries. Furthermore, Menkin [29] has recently shown that extract of adrenal cortex inhibits the dilatation of capillaries which usually results from the cutaneous injection of leukotaxine or exudates. The significance of these observations in relation to adrenal cortex insufficiency is not yet apparent.

TREATMENT OF ADRENAL CORTEX INSUFFICIENCY

The treatment of adrenal cortex insufficiency and that of diabetes mellitus have much in common. In both diseases therapy should be directed toward (1) the specific replacement of the hormone or hormones lacking, (2) the correction of the physiologic disturbances resulting from hormonal deficiencies and (3) the avoidance of those factors known to intensify the abnormalities present. The treatment of adrenal cortex insufficiency as exemplified by Addison's disease is also analogous to that of diabetes in that often a few simple measures suffice to control the disease, whereas at times the failure to institute vigorous therapeutic measures promptly may result in a fatal outcome which might have been avoided. Thus, in a patient whose symptoms and signs of adrenal cortex insufficiency are mild, ingestion of a moderate amount of salt in addition to that present in the diet, moderate limitation of the potassium content of the diet, avoidance of extremes of heat and cold, as well as avoidance of mental and physical strain, may be adequate to maintain moderately good health for months or years. On the other hand, when a crisis develops either in the natural course of the disease or because of salt withdrawal, diarrhea, acute infection, surgical intervention or other factors, an immediate intensive attempt to restore base and water by all possible means becomes imperative to avoid fatal peripheral circulatory collapse.

In recent years the treatment of Addison's disease has been advanced materially through (1) the introduction of salt therapy, (2) the restriction of potassium salts, (3) the elaboration of extracts of the adrenal cortex and (4) the synthesis and availability of desoxycorticosterone esters. The role of each of these must be considered in detail.

Role of Salt and Diet.—With the ingestion of 7 to 20 Gm. of salt in addition to that of the diet, many patients with Addison's disease can be restored to moderately good health for months or years, as stated. Most of these patients take their salt in enteric-coated 1.0 Gm. tablets distributed at frequent intervals during the course of the day. Others prefer to take their salt in the form of an approximately 1 per cent solution. Only a few are able to tolerate capsules. Wilder and associates have suggested that part of the sodium be taken in the form of citrate or bicarbonate to avoid chloride retention. In the writer's experience this has rarely proved necessary.

It should be pointed out that before the advent of desoxycorticosterone many patients in severe addisonian crises recovered as a result of the parenteral administration of liberal amounts of physiologic solution of sodium chloride. This treatment not only restored base but also lowered the blood potassium and nonprotein nitrogen to normal, improved renal function, raised the blood pressure and relieved peripheral circulatory collapse.

Wilder and his associates [12] have properly advocated the restriction of potassium in the diet of the salt-treated patients with adrenal cortex insufficiency, and Sister Mary Victor [30] has carefully outlined the technic of the preparation of this type of diet.[31] In view of the capricious appetites of most patients with Addison's disease, the rigid restriction of the intake of potassium becomes more a theoretical than a practical consideration. In patients who cannot be maintained in good health through the ingestion of large amounts of salt and moderate restriction of the intake of potassium, treatment with desoxycorticosterone esters is indicated. The treatment of hypoglycemic episodes occurring in Addison's disease is best accomplished by the ingestion of a glass of orange juice or two lumps of sugar. If the patient is unable to cooperate, 50 cc. of a 25 per cent solution of dextrose may be given intravenously. Infusions of large amounts of dextrose are apt to give rise to hyperglycemia, followed in the course of two to four hours by a recurrence of hypoglycemia.

Desoxycorticosterone Acetate.—Since Steiger and Reichstein [32] synthesized desoxycorticosterone, this natural steroid of the adrenal cortex has become available for the treatment of patients and has initiated a new era in the therapy of adrenal cortex insufficiency. This particular substance, as has been suggested in another chapter, affects almost exclusively electrolyte and water metabolism, as has been demonstrated by the studies of Thorn and his associates,[33] and Cleghorn and his co-workers,[34] Levy Simpson [35] and Loeb and his collaborators [36] (shown in the accompanying chart). It causes striking retention of sodium salts with restoration of the blood sodium level to normal. It also causes retention of water with increase in plasma and interstitial fluid volume and consequent gain in weight. It lowers the serum potassium, at times to abnormally low levels, and temporarily increases the excretion of this ion. It restores renal function and increases the excretion of nitrogen when nonprotein nitrogen has been retained. Desoxycorticosterone esters also cause a decrease in the concentration of total protein, calcium

28. Stahl, Jules; Atchley, D. W., and Loeb, R. F.: Observations on Adrenal Insufficiency, J. Clin. Investigation **15**: 41 (Jan.) 1936.

29. Menkin, Valy: Effect of Adrenal Cortex Extract on Capillary Permeability, Am. J. Physiol. **129**: 691 (June) 1940.

30. Mary Victor, Sister: Directions for the Planning of Diets Low in Content of Potassium, Proc. Staff Meet., Mayo Clin. **12**: 424 (July 7) 1937.

31. The following foods should be rigidly avoided: soups, broths, gravies, catsup, dried fruits and vegetables, bran and molasses. The consumption of milk, meat and leguminous vegetables should be moderately restricted. Meats and vegetables should be cut into small pieces and cooked in 6 to 8 volumes of water.

32. Steiger, Marguerite, and Reichstein, T.: Partial Synthesis of a Crystallized Compound with the Biological Activity of the Adrenal Cortical Hormone, Nature **139**: 925 (May 29) 1937.

33. (*a*) Thorn, G. W.; Howard, R. P.; Emerson, Kendall, Jr., and Firor, W. M.: Treatment of Addison's Disease with Pellets of Crystalline Adrenal Cortical Hormone (Synthetic Desoxy-corticosterone Acetate) Implanted Subcutaneously, Bull. Johns Hopkins Hosp. **64**: 339 (May) 1939. (*b*) Thorn, G. W.; Howard, R. P., and Emerson, Kendall, Jr.: Treatment of Addison's Disease with Desoxy-Corticosterone Acetate, a Synthetic Adrenal Cortical Hormone (Preliminary Report), J. Clin. Investigation **18**: 449 (July) 1939. (*c*) Levy Simpson, S.: Discussion on Recent Developments in the Treatment of Addison's Disease, Proc. Roy. Soc. Med. **32**: 685 (Dec. 13) 1938.

34. Cleghorn, R. A.; Fowler, J. L. A., and Wenzel, J. S.: The Assay of Desoxycorticosterone Acetate and Its Use in the Treatment of Addison's Disease, J. Clin. Investigation **18**: 475 (July) 1939.

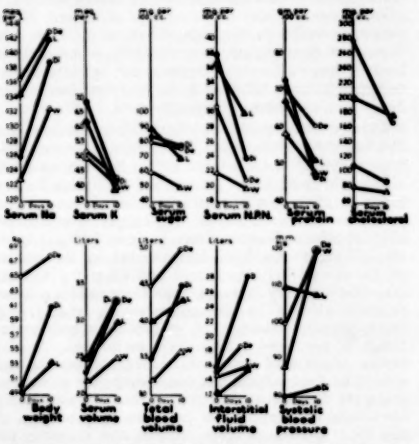
35. Levy Simpson, S.: The Use of Synthetic Desoxycorticosterone Acetate in Addison's Disease, Lancet **2**: 557 (Sept. 3) 1938.

36. (*a*) Loeb, R. F.; Atchley, D. W.; Ferrebee, J. W., and Ragan, Charles: Observations on the Effect of Desoxycorticosterone Esters and Progesterone in Patients with Addison's Disease, Tr. A. Am. Physicians **54**: 285, 1939. (*b*) Ferrebee, J. W.; Ragan, Charles; Atchley, D. W., and Loeb, R. F.: Desoxycorticosterone Esters: Certain Effects in the Treatment of Addison's Disease, J. A. M. A. **113**: 1725 (Nov. 4) 1939.

and cholesterol in the serum, probably because of the hemodilution associated with an increase in plasma volume.

There are great variations in the responses to desoxycorticosterone esters in patients suffering from adrenal cortex insufficiency. These are important to recognize and as yet impossible to anticipate. For example, in studies at the Presbyterian Hospital,[36b] in New York, one patient became markedly edematous and gained 11 Kg. in ten days, during which time he received 10 Gm. of salt a day and 19 mg. of desoxycorticosterone propionate daily. On the other hand, another patient receiving the same diet and the same amount of salt gained but 2 Kg. in thirty days, during which time he received 25 mg. of the same synthetic product each day. Normal persons on this regimen gain but minimal amounts of weight.

The arterial blood pressure of patients with Addison's disease who are treated with desoxycorticosterone esters rises. In conjunction with salt solution administered



Effects produced in patients with Addison's disease in ten days by a desoxycorticosterone derivative. These patients received large doses, i. e., about 190 mg., during the initial ten days of treatment.

during crises, the drug may cause a rise in pressure from shock levels in the course of a few hours. In other patients the rise in blood pressure may be gradual over a period of two to four weeks. At times hypertension may appear. Thus, in four of the patients studied by us there has been a rise in blood pressure to 175/100, 160/92, 160/110 and 146/108 respectively. Whether or not these patients had underlying hypertensive disease, masked by Addison's disease, is not known. It is also not known whether the rise in blood pressure is dependent on factors other than the correction of the disturbances of electrolyte and water metabolism.

An important fact to be borne in mind is that desoxycorticosterone esters have no demonstrable effect on the carbohydrate metabolism of patients with Addison's disease. No definite effect on the fasting blood sugar, dextrose tolerance curves or respiratory quotients has been observed. Furthermore, spontaneous and severe hypoglycemia may appear in patients receiving enough synthetic desoxycorticosterone to correct disturbances of electrolyte and water metabolism, just as it may appear in patients receiving adequate amounts of salt alone. Recent studies [37] of patients receiving other steroids of the adrenal cortex, e. g., corticosterone and compound E of Kendall, as well as cortical extract, indicate that massive doses of these substances have some effect on carbohydrate metabolism. Unfortunately, the amounts of these steroids necessary to produce a significant effect are not available for clinical use, and the amount of cortical extract required to elevate the blood sugar and prevent hypoglycemia is in most cases almost prohibitive.

There is no definite evidence that the pigmentation of the patient with Addison's disease is influenced by desoxycorticosterone esters. It is true that patients under treatment with the synthetic compound and salt appear lighter in color, but it seems likely that this change should be ascribed to rehydration rather than to depigmentation. I have not seen pigment spots in the oral mucous membranes disappear under any form of treatment. Possibly more definite knowledge concerning pigment metabolism will be forthcoming when patients have been under treatment for longer periods.

Subjectively, desoxycorticosterone esters tend to increase the sense of well-being, the strength, the appetite and the outlook on life of patients with Addison's disease. A number of patients resume work, and many others are able, from the standpoint of strength, to take up normal activities. It must be remembered, however, that the majority of patients with Addison's disease suffer from tuberculous infection, and this constitutes a therapeutic problem in itself.

Administration of Desoxycorticosterone Esters.—Two general technics for the treatment of adrenal cortex insufficiency with desoxycorticosterone acetate or propionate have been developed. Thorn and his co-workers [38a] and Levy Simpson [38c] have prepared and implanted subcutaneously, with great success, pellets of a crystalline preparation (synthetic desoxycorticosterone acetate). Others [38] have administered desoxycorticosterone esters subcutaneously or intramuscularly in solutions of peanut or sesame oil. Desoxycorticosterone is only sparingly soluble in water and is essentially without effect when patients with Addison's disease take it by mouth.

The preparation of pellets for implantation presents two problems. The first is that of sterility, which is difficult to obtain, because high temperatures destroy the compound. The second problem is concerned with the pressure under which pellets are prepared. If they are too solidly packed, their solubility is slight. If they are too loosely packed, absorption is apt to be irregular and, indeed, if they crumble, absorption may be very rapid, and serious overdosage may ensue. Thorn [38a] has prepared and standardized his pellets so that from each is dissolved 0.3 to 0.4 mg. of desoxycorticosterone acetate daily. After the daily requirement of the substance is determined in the patient with Addison's disease who takes about 4 Gm. of salt a day in addition to that of a normal diet, by means of daily subcutaneous injections of desoxycorticosterone acetate, the pellets are implanted subcutaneously below the scapula. Enough pellets are used so that the number implanted will yield about two thirds of the subcutaneous requirement. This procedure allows a margin of safety in that if the pellets produce symptoms or signs of overdosage, the salt intake may be reduced. If the

37. Thorn.[38] Ferrebee and others.[38]

38. Wilder, R. M.: Progress in Treatment of Addison's Disease, Proc. Staff Meet., Mayo Clin. **15**: 273 (May 1) 1940. Levy Simpson.[38] Ferrebee and others.[38]

pellets are not quite enough to maintain the sodium concentration of the blood at a normal level, the salt intake may be increased, or supplementary doses of desoxycorticosterone acetate may be injected, or more pellets may be implanted.

When patients are treated with daily subcutaneous injections instead of pellets, they are trained in the technic of injection as are diabetic patients who take insulin. The patients in our experience [36b] do best on a normal diet of average salt content, and the dose of desoxycorticosterone ester is adjusted under these conditions.

Patients should be under close observation during the regulation of their dosage. They should be weighed daily and their blood sodium, serum protein, potassium, nonprotein nitrogen and sugar should be determined initially if possible. The vital capacity, the venous pressure and the size of the heart as determined by roentgen examination should be observed from time to time, as these examinations and auscultation of the chest afford the best evidence of impending cardiac insufficiency, a complication occasionally occurring in the course of treatment.

The maintenance requirements of desoxycorticosterone acetate or propionate vary greatly in different patients. In our series the dose necessary to maintain the normal blood electrolyte pattern has varied from 1 mg. to 7 mg. daily.

In the presence of a crisis or at the beginning of treatment in the presence of moderately severe insufficiency, larger doses may be required for two or three days. A dose of 15 mg. may perhaps be given safely twice a day, provided the patient is carefully watched for evidence of overdosage. In the presence of a severe crisis the administration of desoxycorticosterone acetate should be supplemented by one or two daily infusions of 1,500 cc. of physiologic solution of sodium chloride until the patient is able to take food and fluid by mouth. No further definite rules can be advanced for the treatment of the patient in a crisis, as the desoxycorticosterone and salt requirements differ widely not only in different patients but also in the same individual at different times.

Surgical Procedures.—Before the advent of desoxycorticosterone acetate, major surgical operations in patients with Addison's disease almost invariably proved fatal. At the present time an operation may be undertaken with comparative safety if the disturbances of electrolyte and water metabolism are first corrected with synthetic desoxycorticosterone. No specific regimen for anteoperative therapy can be outlined, but in some instances the injection of 25 mg. of desoxycorticosterone acetate four hours before operation and perhaps 1 liter of saline solution serves to prevent serious depletion and consequent shock. In the postoperative period the patient must be watched for evidence of adrenal cortex insufficiency, including hypoglycemia, as well as for manifestations of overdosage. The amounts of desoxycorticosterone and salt must be adjusted to these indications.

Complications.—Desoxycorticosterone esters which produce the striking salutary effects described in patients with adrenal cortex insufficiency may at times give rise to dangerous complications. Among the first 18 patients whom we [36] treated with the synthetic substance at the Presbyterian Hospital there were 15 in whom edema developed, varying from transient puffiness of the face or ankles to massive anasarca. In 5 of these patients there developed also varying degrees of respiratory distress and a sense of tightness of the chest associated with roentgen evidence of dilatation of the heart, predominantly on the right side. In some of these patients there occurred an elevation of venous pressure, roentgen and clinical evidence of pulmonary congestion and a decrease in vital capacity. Cardiac insufficiency developing as a consequence of desoxycorticosterone therapy has been observed also by others. This complication of therapy is fortunately reversible in most instances but may prove fatal. The mechanisms responsible for the development of cardiac insufficiency have not been definitely established. Arterial hypertension cannot be of great importance, as congestive failure appeared in 3 patients in whom the systolic pressure was below 110 mm. of mercury. An increase in plasma volume and a decrease in the serum potassium concentration may be of importance. It is of interest that Ragan,[39] at the Presbyterian Hospital, has been able to produce cardiac dilatation in adrenalectomized dogs by massive doses of desoxycorticosterone acetate and sodium chloride, but he has observed no effect in normal animals.

Not only have patients under treatment with desoxycorticosterone esters suffered from varying degrees of cardiac insufficiency, but in our series 6 of 20 patients given this therapy in the last twelve months have died. Of these, 1 died of cardiac insufficiency, 1 died of disseminated tuberculosis and 1 died at home presumably of adrenal cortex insufficiency when the dose of the synthetic compound was reduced excessively for the relief of mild symptoms of cardiac insufficiency. Two other patients died suddenly at home without the cause of death being determined. Finally, a patient died suddenly while under observation in the hospital. She had mild cardiac insufficiency and mild hypoglycemia (blood sugar 62 mg. per hundred cubic centimeters). Her blood sodium and potassium had been normal three days before death, and at autopsy no adequate cause for her sudden demise was determined. Our experiences are entirely similar to those recently reported by Wilder [38] and by Thompson and co-workers.[40]

Thus, it is apparent that while desoxycorticosterone therapy has proved exceedingly useful, it is not devoid of danger. Furthermore, it should not be considered a panacea in the treatment of the numerous disturbances present in adrenal cortex insufficiency. It has been shown to have no demonstrable effect on carbohydrate metabolism in patients with adrenal cortex insufficiency and no definite effect on pigmentation. It does not completely relieve the symptom of adynamia, as might be anticipated from Ingle's study.[26] Finally, a number of patients, apparently adequately controlled from the standpoint of electrolyte and water metabolism, died rather suddenly and for no obvious cause. Excessive doses of desoxycorticosterone cause a periodic paralysis associated with a sharp decrease in blood potassium. This paralysis is relieved by the administration of potassium chloride. It is possible that sudden weakness appearing in patients treated with synthetic hormone may, at times, have a similar basis.

Adrenal Cortex Extract.—Commercial preparations of adrenal cortex have, in large amounts, been shown to have definite effects on water and electrolyte [41] as

39. Ragan, Charles: Unpublished data.
40. Thompson, W. O.; Thompson, Phebe K.; Taylor, S. G., and Hoffman, W. S.: Treatment of Addison's Disease with Desoxycorticosterone Acetate, abstr. J. A. M. A. 114:668 (Feb. 24) 1940.
41. Thorn, G. W.; Garbutt, H. R.; Hitchcock, F. A., and Hartman, F. A.: The Effect of Cortin on the Sodium, Potassium, Chloride, Inorganic Phosphorus and Total Nitrogen Balance in Normal Subjects and in Patients with Addison's Disease, Endocrinology 21:202 (March) 1937.

well as carbohydrate metabolism. The effects are, however, small, and it seems unlikely, as stated before, that these extracts in the doses usually administered have significant clinical value. On theoretical grounds, extract of adrenal cortex should prove of greater value than desoxycorticosterone, as it contains other steroids which are known to have greater and more diversified action, particularly in relation to carbohydrate metabolism. Unfortunately, the concentrations of these steroids are not sufficiently high to prove of real value in small doses. On the basis of our studies [25] it does not seem probable that doses of less than 5 cc. of cortical extract contain clinically significant quantities of steroids that would affect the carbohydrate metabolism. Consequently, the injection of 5 cc. amounts of extract, even in conjunction with the administration of desoxycorticosterone acetate, does not seem indicated in the maintenance of the patient.

Despite these criticisms, it seems probable that 50 to 75 cc. at least of commercial extract given in divided doses in the course of twenty-four hours in addition to saline infusions and with repetition of the dosage the next day may prove more satisfactory in treating serious crises than will desoxycorticosterone acetate alone.

Although cortical extracts have been shown to be active when administered by mouth, the amounts necessary are probably at least 3 to 4 times that of the parenteral dose. Consequently oral administration is of doubtful clinical value.

Studies on adrenalectomized animals have shown that a number of preparations of adrenal cortex extract have demonstrable potency when administered orally. Pfiffner and his co-workers [41a] estimated that 10 cc. of their preparation given by mouth was equivalent to about 1 cc. given parenterally. Thorn [41b] demonstrated that the glycerin extract of 1,000 Gm. of adrenal glands administered by mouth daily to a 10 Kg. adrenalectomized dog maintained the animal in good health. Grollman[41c] has also reported activity of a charcoal adsorbate of adrenal cortex extract. On the basis of these and similar findings the oral administration of extracts has been recommended in the treatment of patients. In view of the relative inactivity of the usual cortical extracts administered parenterally in doses of 5 cc. or less, it is unlikely that considerably larger amounts given by mouth have any significant therapeutic effect. The observations of the writer support this view. Thus one patient was given oral doses of a commercial glycerin extract costing from $5 to $15 a day over a period of some months. The extract was given in addition to salt and had little if any clinical effect. This patient's disease is now easily controlled by small doses of desoxycorticosterone acetate. Another patient whose disease was controlled both by desoxycorticosterone acetate in doses of 1 to 2 mg. daily and by about 15 Gm. of salt was given 15 tablets of an oral preparation in conjunction with vitamin C daily. When the salt intake was reduced to 5 Gm. a day, symptoms of acute insufficiency developed in three days with a fall in sodium from 136 to 129 m. eq. per l. despite the large dose of oral extract. A third patient taking 6 tablets of the same preparation and 3 Gm. of salt a day in addition to her diet was admitted to the hospital because of progressive weakness, anorexia and nausea. Her blood sodium on admission was 124.8 m. eq. per liter. A single infusion of salt solution, the discontinuation of the oral cortical extract preparation and an increase in the daily salt intake to 12 Gm. a day for four days resulted in clinical improvement associated with a rise in blood sodium to 135 m. eq. per liter. It is the writer's opinion that, in the presence of established adrenal insufficiency, cortical extract given by mouth has no place in treatment, particularly now that desoxycorticosterone acetate is available.

Numerous attempts have been made to transplant an adrenal gland or the cortical cells of a gland from one person to another in the treatment of Addison's disease. These efforts have not met with success up to the present time, and the procedure is not to be recommended. Ingle has devised an ingenious method for the successful transplantation of the adrenal glands of a newborn rat into another young rat, but this procedure is so far only of academic interest. Auslender [42] has recently reported successful heterotransplants of adrenal cortex free from medullary cells. These observations have not been confirmed.

TREATMENT OF MISCELLANEOUS CONDITIONS

Preparations of the adrenal cortex have been employed in recent years in the treatment of various conditions ranging from nonspecific fatigue to surgical shock. At the present time it is difficult to appraise the value or wisdom of administering these preparations in the absence of demonstrable adrenal cortex insufficiency, since their continued administration is known to cause atrophy of the adrenal glands of normal animals.[43] However, Perla and his co-workers [44] have offered evidence suggesting that anteoperative treatment with saline solution and desoxycorticosterone acetate prevents surgical shock, and Scudder [45] has advocated the use of large quantities of extract of adrenal cortex in the treatment of that condition. These studies receive theoretical support from the observations of McAllister [46] and of Ragan and his associates.[47] These workers have shown that desoxycorticosterone esters administered three to six hours before operation prevent the usual decrease in plasma volume accompanying ether anesthesia and surgical operation.

Weil and Browne [48] reported that the urinary substances protecting young adrenalectomized rats from the fatal effects of exposure to cold are not excreted by normal human beings but appear in the urine following febrile illnesses and other forms of stress. Although the significance of this report is not yet apparent, it does not justify indiscriminate administration of preparations of the adrenal cortex.

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Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING CHAPTER, WHICH IS THE SIXTH OF A SERIES ON AMPUTATIONS AND ARTIFICIAL LIMBS TO APPEAR IN THIS COLUMN. WHEN COMPLETED, THE SERIES WILL BE PUBLISHED IN THE FORM OF A HANDBOOK ON AMPUTATIONS. THE COUNCIL WISHES TO EXPRESS ITS APPRECIATION FOR THE COOPERATION OF ITS GROUP OF CONSULTANTS ON ARTIFICIAL LIMBS. THE COUNCIL IS REPRESENTED BY DRS. FRANK D. DICKSON, HARRY E. MOCK, FRANK R. OBER, S. PERRY ROGERS, PAUL STEELE AND PHILIP WILSON, AND THE ASSOCIATION OF LIMB MANUFACTURERS OF AMERICA IS REPRESENTED BY MESSRS. MCCARTHY HANGER SR., W. E. ISLE, JOSEPH A. SPIEVAK, DAVID E. STOLPE AND J. B. KORRADY.

HOWARD A. CARTER, Secretary.

CHAPTER II—SECTION V

REAMPUTATIONS AND SECONDARY OPERATIONS

Careful adherence to the general principles involved in amputations will prevent or lessen the need for reamputations. Nevertheless, in the hands of the best surgeons reamputation is occasionally necessary. Reoperations on the stump are more often needed. The following conditions are the commonest causes for these secondary operations and reamputations:

1. *Sloughing or Ulceration Over the End of the Stump.*—In spite of the most careful technic the posterior fascial flap, in leg amputations, may become detached from the bone, leaving the tibia covered only by skin. Ulceration at this point occurs and sloughing may result in leaving a portion of the tibia exposed. Again infection occasionally develops in the soft tissues of the stump, necessitating removal of sutures and retraction of the skin and fascial flaps with resulting exposure of the end of the tibia. In lower leg amputations done because of circulatory disease or for diabetes, one cannot use too long an anterior flap lest it tend to undergo necrosis along its margin. It is exceedingly difficult to do plastic skin operations on a stump with the bone thus exposed. It is far wiser to reopen the stump by cutting away the ulcerated portion and reforming the best possible flaps, saw away the exposed portion of bone and treat it as one would at a primary amputation. Reamputation of the fibula at a suitable level, reinjection of exposed nerves and religation of major vessels are indicated. These complications usually arise in leg stumps which were originally cut too long, so that reamputation frequently provides a stump capable of better function than the original. When the stump is 8 or 10 inches below the knee, the reamputation may be performed 3 to 5 inches higher, thus providing better flaps with a better selection for the location of the scar. Fortunately a stump 5 or 6 inches in length gives better healing and better leverage for the use of the prosthesis than does the original 8 or 10 inch stump. There is less tendency toward sloughing of the flap when the original operation is performed in these higher sites. The usual mistake which so often necessitates these reamputations is our effort to leave a long lower leg stump.

2. *Cutaneous Defects Over the Sides of the Stump.*—When the ulceration occurs on the side of the stump and not directly over the bone, it is usually caused by impairment of circulation due to too tight a flap. It may also be due to pressure of a socket on soft tissues that are too bulky or redundant. Such areas may be dissected away, allowed to form a good granulation bed and then skin grafted. Skin grafts are satisfactory, however, only if the area is one not subjected to pressure within the socket. Plastic operations with the formation of pedicled flaps from skin adjacent to the stump may be used, provided the site of the pedicled graft can be closed by primary suture and is not itself subjected to pressure from the socket. Pedicled grafts from the opposite extremity are occasionally indicated. Unless infection is very mild or absent, the site of defect must be carefully cut away and the wound allowed to granulate and become healthy before the graft is applied. Redundance of skin and soft tissues may be excised and closed by primary suture with excellent results provided the scar is placed at a point not subjected to pressure within the prosthesis.

3. *Osteomyelitis or Aseptic Necrosis of the End of the Bone.*—It is unusual for an active, suppurating type of osteomyelitis to occur; an aseptic necrosis or low grade osteomyelitis is more common. A severe infection is opened and packed like any osteomyelitis. In the absence of severe infection, clean excision of all dead tissues and reamputation may be performed. Fresh flaps should be dissected free of their original scars and all important structures dealt with as in a primary amputation. Special care is needed to avoid redundance of soft tissues.

4. *Neuromas.*—Painful stumps are usually due to nerves caught in scar tissue or to typical neuromas. Seldom is reamputation for this condition necessary. However, when one is convinced that the painful stump is real, exploration of the scars or direct attack on the neuroma is indicated. The offending nerve is carefully dissected from the surrounding tissue, cut away higher up and the end of the nerve injected with absolute alcohol.

5. *Neuroses.*—Neuroses of all descriptions frequently develop with the symptoms referred to the stump or even to the amputated member. True malingering in a case of amputation is exceedingly rare. One must not be too prone to jump to the conclusion that the patient's complaints are of a neurotic order. A minute nerve caught in a scar can give the pain, twitching sensation or even the picture of causalgia so often complained of. Furthermore, reoperations do not always disclose or remove the cause. One must approach these cases with a sympathetic understanding rather than a brusque statement that the patient only imagines the complaint. These cases are problems for both the surgeon and the fitter of the artificial limb, who is often unjustly accused for the complaints. Before considering reamputation because of a painful stump and before recommending the purchase of a new artificial limb for the cure of a similar complaint, one must rule out a true neurosis as the cause of symptoms. Conversely, the surgeon must be very careful in his remarks to the patient complaining of pain in the stump or in his criticism of the prosthesis worn lest inadvertently he sow seeds of neurosis in the mind of a susceptible individual.

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.

HOWARD A. CARTER, Secretary.

AN APPRECIATION

The Council on Physical Therapy is most desirous of expressing its sincere appreciation to the following consultants who have given so generously of their time and effort during the past year in assisting the Council in its work:

Drs. Fred L. Adair, Howard Ballenger, M. Herbert Barker, Walter M. Boothby, Milton B. Cohen, W. Allen Conroy, Earl C. Elkins, Samuel Feinberg, Hart Fisher, Hubert H. Hathaway, John S. Hibben, Archibald Hoyne, K. K. Jones, Louis Katz, Disraeli Kobak, Arno Luckhardt, Harry E. Mock Jr., C. O. Molander, Tell Nelson, Benjamin Orndoff, S. L. Osborne, George Shambaugh Jr., William O'Neill Sherman, E. M. Smith, Kellogg Speed and Grant E. Ward.

Audiometers and Hearing Aids.—Drs. C. C. Bunch, George M. Coates, E. P. Fowler, Isaac Jones, Douglas Macfarlan, C. Stewart Nash, Horace Newhart, Paul Sabine, B. R. Shurly and W. P. Wherry.

Educational Work.—Drs. Frances Baker, Benjamin Boynton, Muriel Case Downer, F. H. Ewerhardt, Richard Kovacs, Fred B. Moor, W. H. Northway, Walter M. Solomon, Arthur L. Watkins and Walter J. Zeiter.

Roentgen Rays.—Drs. William E. Chamberlain, Arthur C. Christie, E. C. Ernst, Gioacchino Failla, F. M. Hodges, John T. Murphy, Robert C. Newell, Eugene Pendergrass, U. V. Portmann, Lauriston S. Taylor and J. L. Weatherwax.

Artificial Limbs.—Drs. S. Perry Rogers, Paul Steele and Philip Wilson, and Messrs. McCarthy Hanger Sr., W. E. Isle, J. B. Korrady, Joseph Spievak and David E. Stolpe.

Electrocardiographs.—Drs. A. R. Barnes, George Fahr, Harold E. B. Pardee, W. D. Stroud, Carl J. Wiggers and Frank N. Wilson.

NEWMAN THERMO-FLO ACCEPTABLE

Manufacturer: Majestic Surgical Instrument Company, 2608 Cicero Avenue, Chicago.

The Newman Thermo-Flo is designed to be used for the intravaginal application of superheated air. In operation, heated air is circulated through a specially shaped thin-walled rubber bag, which is inserted in the vagina in a collapsed state and then inflated with air so as to distend the vagina. The rubber bag is brought into contact with the tissues, and heat is conducted over a large area to the surrounding tissues.

Newman Thermo-Flo.

The apparatus consists essentially of a fan which circulates air through the applicator bag, an electrical unit which heats the air, a thermostat for controlling the temperature (temperatures up to 130 F. may be obtained), a thermometer which extends through the applicator and into the bag, and a hand-operated rubber bulb used to inflate the rubber bag. The pressure, approximately ½ to ¾ pound, is indicated on the pressure gage mounted on the control panel.

As evidence of its therapeutic usefulness, the firm submitted a summary of the results of 402 cases treated with the Thermo-Flo at a maternity hospital and a detailed report of 71 patients having chronic inflammatory disease of the pelvic organs who were treated with the Thermo-Flo in the department of obstetrics and gynecology of a university hospital.

The maternity hospital reported its results with the Newman Thermo-Flo as follows:

Summary of results with the Thermo-Flo Machine in cases of:

I. Acute salpingitis—gonorrheal in origin.
II. Subacute salpingitis—gonorrheal in origin.
III. Chronic salpingitis: A—with small palpable mass.
B—with large palpable mass.
IV. Subacute pelvic cellulitis—postpartum and postabortal probably streptococcic in origin.
V. Chronic pelvic cellulitis—postpartum and postabortal in origin.
VI. Endometriosis.

The following table summarizes the results obtained: (The Roman numerals in the chart correspond to those used in the preceding table.)

Diagnosis	No. of Cases	Good No.	Good Per Cent	Fair No.	Fair Per Cent	Poor No.	Poor Per Cent	Satisfactory per Cent, Good or Fair	Surgery No.	Surgery Per Cent
I	33	12	36.3	13	39.3	8	24.4	75.6	0	0
II	21	5	23.8	6	28.6	10	47.6	52.4	2	9.5
IIIA	190	72	38.1	86	45.5	31	16.4	83.6	29	15.3
IIIB	114	24	21.2	49	42.1	42	36.7	63.3	9	7.9
IV	10	2	20.0	3	30.0	5	50.0	50.0	0	0
V	23	4	17.4	12	52.2	7	30.4	69.6	4	17.3
VI	12	0	0	0	0	12	100.0	0	12	100.0
Total	403	119	29.6	168	42.0	115	28.4	71.6	56	13.9

The report from the university hospital contained the following data:

Results

Group 1
Chronic bilateral salpingo-oophoritis—39 cases
Complete cure 6
Marked improvement 25
Moderate improvement 5
Slight or no improvement 3
Three patients in this group became pregnant after the treatments were completed.

Group 2
Chronic bilateral salpingo-oophoritis with unilateral or bilateral tuboovarian masses—13 cases
Complete cure 0
Marked improvement 10
Moderate improvement 1
Slight or no improvement 2

Group 3
Postoperative residual pelvic inflammatory disease—7 cases
Complete cure 1
Marked improvement 5
Moderate improvement 0
Slight or no improvement 1

Group 4
Chronic parametritis—7 cases. (4 postabortive. 2 postpartum, 1 postoperative.)
Complete cure 1
Marked improvement 5
Moderate improvement 1
Slight or no improvement 5

Group 5
Chronic pelvic inflammatory disease (frozen pelvis)—5 cases
Complete cure 0
Marked improvement 4
Moderate improvement 1
Slight or no improvement 0
One patient in this group became pregnant after the treatments were completed.

Summary of Results

Complete cure ..... 57 cases (80.3%)
Marked improvement (included with cases of "complete cure")
Moderate improvement ..... 8 cases (11.3%)
Slight or no improvement ..... 6 cases (8.4%)
(Interpretation of terms):
Complete cure: Symptomatic and anatomic cure.
Marked improvement: Complete disappearance of symptoms with definite anatomic improvements.
Moderate improvement: Symptomatic improvement with little anatomic regression.
Slight or no improvement: Slight or no improvement either symptomatically or anatomically.

A detailed description of each of the 71 cases was given in the report.

The apparatus was investigated clinically by the Council, and it was found to be satisfactory from the treatment standpoint. The thermostat seemed to control the air temperatures quite well; at any one setting the temperature of the air in the applicator remained stable. The operating temperature is read on the thermometer in the applicator extending into the bag and is regulated by means of the thermostat on the panel.

The Council voted to accept the Newman Thermo-Flo for inclusion on its list of accepted devices.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.
OFFICE OF THE COUNCIL.

CYCLOPROPANE

In 1939 the Council published a report[1] of its consideration of cyclopropane without special reference to any particular brand. On the basis of the evidence available at that time it was pointed out that the gas is a suitable anesthetic agent when used cautiously by those fully informed of its properties, potential dangers and signs which indicate the stages of anesthesia with the agent. It was emphasized that unusual cardiac effects (arrhythmias) are encountered with cyclopropane, that high concentrations of the gas and its combination with sympathomimetic or other drugs which increase such irregularities are to be avoided and that it is therefore essential to watch the pulse carefully during administration. It was further pointed out that the signs to indicate the depth of anesthesia differ from those of Guedel for other anesthetic agents and that, since the respiratory center is not stimulated by cyclopropane, premedication which affects the respiratory rate should be used with caution because these signs may be further obscured by too large doses. It was indicated that, except for difficulty in detecting the plane of anesthesia by those unfamiliar with the agent, the lack of respiratory stimulation and the tendency to produce cardiac arrhythmias and postanesthetic headache, the gas possesses the advantages of decreased pulmonary irritation, effectiveness in concentrations which provide abundant oxygen, less excitement during induction and low toxicity. From the standpoint of chemical and

1. The present Status of Cyclopropane, J. A. M. A. 113: 1064 (March 8) 1939.

physical properties, it was indicated that cyclopropane has the same potential danger of explosibility as the more commonly used ethyl ether.

Since the previous report of the Council was published, additional clinical and pharmacologic studies of cyclopropane have appeared in the literature.[2]

In general, this further evidence does not alter the previous conclusions of the Council concerning this anesthetic agent. In view of the accumulation of favorable published evidence for the use of cyclopropane as an inhalation anesthetic, the Council was about to give further consideration to a submitted brand of the gas for anesthesia with a view to acceptance when recently reported deaths from explosions of the gas caused the Council to hold acceptance in abeyance pending further investigation of the factors responsible for explosions which have occurred. In the interim cyclopropane had received official recognition under standards included in the U. S. Pharmacopeia (XI, 1939, Second Supplement).

In proceeding with its investigation into the cause of the explosions which have occurred with cyclopropane, the Council recalled that ten years ago a report by Henderson[3] under the auspices of the Committee on Anesthesia Accidents of the American Medical Association pointed out that explosions of anesthetic mixtures do not occur unless fired, and that precautions to avoid electrostatic discharges and other potential ignition factors must be taken. The Council also considered the incidence of anesthetic explosions which has been reported by Woodbridge[4] for ether, ethylene and cyclopropane. This investigator tabulated the results obtained from a questionnaire answered by eighty-seven specialists in anesthesia. The author made no attempt to include all reported explosions in order to secure a representative, unbiased sampling. The explosion rates for these anesthetic agents were found to be respectively 1.73, 2.44 and 3.85 per hundred thousand administrations, but the standard deviations due to chance are of such magnitude that the differences between the rates reported are of no significance. The explosion mortality was found to be only two (one, cyclopropane) for the entire 2½ million cases tabulated.

From information furnished by a consultant of the Council, some of the explosions with cyclopropane which have occurred since its previous report was published (March 8, 1939) are listed in table 1. It should be noted that the list includes five fatalities and does not agree with the Woodbridge[4] report, in which no attempt was made to include all reported explosions. Previously a note in THE JOURNAL[5] indicated that the number of explosions from mixtures of anesthetic gases listed in an excerpt of the report of the Subcommittee on Fires and Explosions of the American Society of Anesthetists, Inc.,[6] probably did not represent all such explosions that have taken place. Study of the available details of the explosions listed in table 1 revealed that those occurring at the University of Michigan and the University of Minnesota had two features in common: the nurse was wearing rubber gloves and the patient was covered with a woolen blanket. The Michigan explosion occurred during the administration of cyclopropane and oxygen diluted with about 50 per cent helium, whereas the Minnesota explosion occurred with a mixture of cyclopropane, oxygen and ether. In the former instance the nonfatal nature of the explosion was attributed to the possibility that the inert gas helium had reduced the force of the explosion. In both instances the production of static electricity was regarded as the immediate cause.

TABLE 1.—*Cyclopropane Explosions*

Place	Time	Outcome
1. Roosevelt Hospital, New York City	March 1939	Patient died
2. Hartford Hospital, Hartford, Conn	Spring 1939	Patient died
3. Emmanuel Hospital, Omaha.....	May 12, 1939	Patient died
4. University of Michigan, Ann Arbor, Mich.....	November 1939	Machine damaged
5. University of Minnesota Hospital Minneapolis	January 1940	Patient died
6. Sloane Hospital for Women, New York	April 1940	Patient died

Consideration was also given to reports concerning the use of so-called inert gases as diluents of anesthetic mixtures to eliminate explosive concentrations and of methods employed to avoid conditions conducive to the discharge of static sparks. A report of the U. S. Department of the Interior by Jones, Kennedy and Thomas[7] presents data obtained with an

2. These were reported by:
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3. Henderson, Landell: The Hazard of Explosion of Anesthetics, J. A. M. A. **94**: 1491 (May 10) 1930.

4. Woodbridge, P. D.: Incidence of Anesthetic Explosions, J. A. M. A. **112**: 2308 (Dec. 23) 1939.

5. Anesthetic Explosions, Queries and Minor Notes, J. A. M. A. **113**: 1055 (Sept. 9) 1939.

6. News Letter of American Society of Anesthetists, Inc. **2**: 3 (April) 1939.

7. Jones, G. W.; Kennedy, R. E., and Thomas, G. J.: Explosive Properties of Cyclopropane: Prevention of Explosions by Dilution with Inert Gases, Bureau of Mines Report of Investigations 3311, May 1940.

explosion-tube apparatus to determine the inflammability of cyclopropane-air-carbon dioxide, nitrogen and helium mixtures, and cyclopropane-oxygen-helium mixtures.

By trial and error the limits of inflammability of the prepared mixtures were determined and averages taken of those mixtures that just propagated and those that just failed to propagate flame. The data obtained for the cyclopropane-air-(nitrogen, helium, carbon dioxide) mixtures show that at least 13.4 volumes of nitrogen are required per volume of cyclopropane to render all mixtures of these gases noninflammable as compared with 14.8 volumes of helium and only 8.0 volumes of carbon dioxide. Although carbon dioxide is thus shown to be superior as a diluent in the prevention of cyclopropane explosions, the authors point out that this obviously cannot be employed in cyclopropane-oxygen anesthetic mixtures because the high concentration required to eliminate explosive hazards of this mixture would produce marked physiologic effects on patients breathing such mixtures. Helium is indicated as the diluent of choice because it is a light gas which can be breathed with less effort than nitrogen, to compensate somewhat for the lowered oxygen content of proposed mixtures, and because gaseous mixtures containing helium are more difficult to ignite by electric discharges than mixtures containing similar percentages of other inert gases. The data presented for the

TABLE 2.—*Promising Mixtures*

Mixture No.	Composition, per Cent by Volume		
	Cyclopropane	Oxygen	Helium
1	15	20	65
2	20	20	60
3	25	25	50
4	30	30	40

cyclopropane-oxygen-helium mixtures indicate that all mixtures containing 3 to 60 per cent cyclopropane may be used safely. Those mixtures which appear to offer the most promise for anesthetic use are given in table 2.

The authors point out that the mask, the apparatus and the patient's lungs will contain explosive mixtures for a very short period both at the beginning and at the end of the administration of the anesthetic and that, while the method of admixture with inert gas eliminates the violently explosive mixtures that usually are present through the anesthesia process, the proper procedure has yet to be worked out for administrating cyclopropane-oxygen-helium mixtures so that explosive mixtures will not be present in the equipment at any time. It is indicated that an extensive program of chemical experiments with nonexplosive mixtures of gaseous combustible anesthetics is in progress. Haas, Hibshman and Romberger[8] have reported similar studies and, on the basis that nitrogen is a satisfactory, readily available diluent gas to render cyclopropane-oxygen anesthetic mixtures nonexplosive, have proposed the use of cyclopropane-air-oxygen for anesthesia by means of an air bulb attachment to the breathing bag for the introduction of air into closed anesthetic machines. At the nineteenth annual meeting of the Congress of Anesthetists held in Chicago, Oct. 21-25, 1940, reports by these and the foregoing investigators included tentative methods for the clinical use of nonexplosive mixtures of cyclopropane. The development of a device for anesthetic machines to detect the presence of explosive concentrations during administration was suggested.

More recently Horton[9] has reported a study of mixtures comprising two anesthetic gases. He is of the opinion that the explosion hazard may be reduced by using mixtures containing cyclopropane, ethylene and oxygen in proper combination. The addition of a fourth gas, such as nitrogen, helium or hydrogen, has been shown to increase the nonexplosive range even further. The use of flame barriers in anesthetic machines to prevent explosion pressures from reaching the patient has been proposed as a third measure to minimize the explosion hazard of anesthetic gases. Evidence that such barriers are feasible has not as yet been offered.

To avoid conditions conducive to the discharge of static sparks it is necessary to have all objects and people in the operating room at the same electrical potential. An advance in this direction has been made by Horton[9] in designing the Horton intercoupler, a high resistance coupling device with five terminals to maintain the same electrostatic potential between any five bodies. The use of high resistance intercoupling is based on the previous report by Woodbridge, Horton and Connell.[10] The problem of static electricity is resolved to the elimination of nonconductors between anesthetic machines and operating room tables and floors and the patient and personnel to dissipate electrostatic charges as rapidly as these develop.

It should be kept in mind that the use of diluent gases to eliminate explosive anesthetic mixtures is limited by the extent to which the oxygen concentration of such mixtures may be reduced without interference with physiologic requirements. From the standpoint of explosion, hydrogen should not be regarded as an inert gas. It is further pointed out that nitrous oxide as well as oxygen supports combustion and therefore that, while a nitrous oxide-oxygen anesthetic mixture alone is relatively safe from the standpoint of explosion, it should not be regarded as a safeguard against this hazard when combined with ether, ethylene or cyclopropane. It should be emphasized that with the exception of nitrous oxide anesthesia the explosive potentialities of anesthetic mixtures of cyclopropane are not greater than those of other commonly employed anesthetics and that precautions to avoid this hazard are the same for all other inflammable anesthetic agents. The use of intercouplers or other means to avoid conditions favoring the discharge of static sparks may be an added hazard unless constant vigilance is applied to the proper technic of their use and the control of all other related factors. It is further emphasized that the Council does not, by this report, recognize the use of any specific mixture of gases in the administration of cyclopropane. The use of diluent gases to eliminate explosive anesthetic mixtures of cyclopropane or other anesthetic agents is in the experimental stage and should not take precedence over proper measures to eliminate all ignition factors.

After further consideration, the Council decided that explosions with cyclopropane are not primarily due to chemical or physical peculiarities of the gas itself but, as with other anesthetic agents, are directly attributable to accidental ignition, the conditions conducive to which may be avoided by observance of the necessary precautions. In view of this and the recent advances made toward the elimination of explosive anesthetic mixtures, it was voted that cyclopropane be accepted with all necessary safeguards.

CYCLOPROPANE FOR ANESTHESIA
(Ohio Chemical & Mfg. Co.)

The Ohio Chemical and Manufacturing Company was first to submit a brand of cyclopropane for the consideration of the Council. A preliminary report of its consideration of this brand was published in 1936.[1] At that time the Council voted to defer further consideration of the agent until more evidence of its usefulness was available.

Subsequently, with the accumulation of the additional clinical and pharmacologic evidence considered in the further report of the Council on the gas published in 1939 without reference to particular brands, it was voted to accept the manufacturer's brand of cyclopropane provided it emphasize in its advertising that the product be employed only by those who are thoroughly familiar with the anesthetic agent and include an adequate description of the cardiac arrhythmias encountered with its use and a cautionary statement to avoid the simultaneous use of epinephrine or related substances.

8. Haas, H. B.; Hibshman, H. J., and Romberger, F. T.: Cyclopropane-Air-Oxygen Anesthesia: A Preliminary Report, Anesthesiol. **1**: 31 (July) 1940.

9. Horton, J. W.: Hazards in the Use of Explosive Anesthetics, Bull. Am. Assn. Nurse Anesthetists **8**: 285 (Nov.) 1940.

10. Woodbridge, P. D.; Horton, J. W., and Connell, Karl: Prevention of Ignition of Anesthetic Gases by Static Spark, J. A. M. A. **113**: 740 (Aug. 26) 1939.

1. Cyclopropane for Anesthesia (Ohio Chemical & Mfg. Co.), J. A. M. A. **106**: 292 (Jan. 25) 1936.

The Ohio Chemical & Manufacturing Company was asked if it wished to have its brand of cyclopropane reconsidered by the Council under these conditions. The company indicated its desire to have the product reconsidered and submitted its current advertising. The manufacturer stated that this brand of cyclopropane is now prepared in conformance to official standards for the gas which had become available in the U. S. Pharmacopeia (XI, 1939, Second Supplement). The advertising was found to require some revision. Accordingly, the Council was about to recommend acceptance of the product when recent explosions with the gas caused the Council to hold acceptance in abeyance pending investigation into the factors responsible for these accidents. The Council voted, however, to give further consideration to the manufacturer's brand of the gas provided it agreed to revise its advertising and the product was found to conform to the official standards.

The manufacturer was notified of this action of the Council and replied that steps were being taken to devise means to avoid the explosion hazard through the development of methods to eliminate the causative factors. The company indicated that the problem was being approached from two angles—(1) the use of inert gas to eliminate explosive concentration of oxygen in cyclopropane anesthesia and (2) the avoidance of conditions conducive to the discharge of static sparks. The manufacturer submitted revised advertising but offered to withhold printing of this pending the favorable outcome of methods developed to eliminate the explosion hazard.

After further consideration of evidence submitted by the manufacturer and the reports in the literature, the Council decided that the explosion hazard of cyclopropane is not due to peculiarities of the gas itesli but, as with other anesthetic agents, is directly attributable to accidental ignition, the conditions conducive to which may be avoided by observance of the necessary precautions. In view of this and the recent advances made toward the elimination of explosive anesthetic mixtures through the use of diluent gases, the Council voted to recognize cyclopropane as an anesthetic agent if used with all necessary safeguards.

In accordance with its decision to accept cyclopropane, the Council has given further consideration to the manufacturer's product. The submitted advertising is found to require only slight further revision. The cooperative attitude of the concern was commended. The Council voted to accept the brand Cyclopropane for Anesthesia (Ohio Chemical & Mfg. Co.) provided advertising is further revised as indicated and the product is found to conform to the standards of the U. S. Pharmacopeia.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

OFFICE OF THE COUNCIL.

CYCLOPROPANE. — Cyclopropanum. — Trimethylene. — C_3H_6.—"Contains not less than 99 per cent by volume of $CH_2CH_2CH_2$."—U. S. P.

For standards see the U. S. Pharmacopeia under Cyclopropanum.

Caution.—Cyclopropane is inflammable and its mixture with oxygen or air will explode when brought in contact with a flame or an electric spark.

Actions and Uses.—Cyclopropane differs from other gaseous anesthetic agents in that the anesthetic-oxygen ratio is reversed —15 per cent of cyclopropane to 85 per cent of oxygen up to the rarely and briefly used 40 per cent of cyclopropane and 60 per cent oxygen. The high anesthetic potency of cyclopropane as compared with other hydrocarbons makes its use advantageous from the standpoint that abundant concentrations of oxygen may be used. There is evidence to indicate that the rate of diffusion of cyclopropane is about twice that of ethylene. Cyclopropane is eliminated less rapidly than ethylene but much faster than ether. Induction and recovery with cyclopropane are therefore slower than with ethylene but more rapid than with ether.

There is some evidence to indicate that cyclopropane affects the autonomic tissue of the heart more than ether or chloroform. In high concentrations it heightens the irritability of this tissue and predisposes to the occurrence of cardiac arrhythmias. This effect has been shown to be enhanced with the simultaneous use of epinephrine. For these reasons the pulse must be carefully observed and the use of sympathomimetic drugs avoided during cyclopropane anesthesia. Cyclopropane does not stimulate respiration as do many other general anesthetic agents, and for this reason preoperative sedation with respiratory depressants must be used with caution. The signs of Guedel for other anesthetic agents do not apply to cyclopropane, so that familiarity with the signs of the stages of anesthesia for cyclopropane is absolutely essential in the administration of this agent.

The explosibility of cyclopropane-oxygen mixtures is not greater than that of other anesthetic-oxygen mixtures with the exception of nitrous oxide, but, since the latter gas also supports combustion, its use with cyclopropane should not be regarded as a safeguard against this hazard. Careful operating room technic to avoid conditions conducive to the production of electrostatic sparks and the presence of open flames and the cautery should be observed with the same precautions as those for other anesthetics.

The advantages of cyclopropane consist in its effectiveness in concentrations providing an adequate supply of oxygen, decreased pulmonary irritation, less excitement during induction and low toxicity. Its disadvantages include lack of respiratory stimulation, difficulty in detection of the planes of anesthesia by those unfamiliar in its administration, and tendency to produce cardiac arrhythmias and postanesthetic headache.

Dosage.—Cyclopropane is usually furnished in compressed form in metal containers. In use the gas is passed into an inhalation apparatus of the closed circuit type and is then administered by inhalation from a rebreathing bag, usually with the admixture of oxygen. The concentration employed varies from 15 to 40 per cent and with the individual patient but should probably not exceed 30 per cent. The remainder of the mixture should consist of a minimum of 20 per cent oxygen, but this should be supplied in quantities adequate for physiologic needs. When other anesthetics are used in combination or when premedication has been employed, less cyclopropane is required.

SOLUTION LIVER EXTRACT-LILLY.—A sterile aqueous solution containing the nitrogenous nonprotein fraction G of Cohn et al. preserved with 0.5 per cent phenol. The potency of the preparation is such that its daily parenteral administration has been found to produce the standard reticulocyte response defined for each U. S. P. unit (injectable) present, when assayed in cases of pernicious anemia as required by the Council.

Actions and Uses.—Solution liver extract-Lilly is proposed for intramuscular injection in the treatment of pernicious anemia. See preceding article, Liver and Stomach Preparations.

Dosage.—In the average uncomplicated case of pernicious anemia in relapse a satisfactory response may be obtained with an initial dose of 5 to 20 U. S. P. units (injectable) daily for the first two or three days, after which weekly injections of 7 to 15 U. S. P. units (injectable) should be continued until the blood picture has returned to normal.

For maintenance of the average uncomplicated case after the normal picture has been established, a minimum of 1 U. S. P. unit (injectable) daily is usually sufficient and may be given as a cumulative dose. Patients exhibiting extensive neurologic involvement or other degenerative changes often require more than this average dose.

Manufactured by Eli Lilly & Co., Indianapolis. No U. S. patent or trademark.

Solution Liver Extract-Lilly, 2 U. S. P. Units per cc., 3.5 cc.: Marketed in rubber stoppered ampules for parenteral administration.

Solution Liver Extract-Lilly, 2 U. S. P. Units per cc., 10 cc.: Marketed in rubber stoppered ampules for parenteral administration.

Solution Liver Extract-Lilly, 1 U. S. P. Unit per cc., 10 cc.: Marketed in rubber stoppered ampules for parenteral administration.

Solution liver extract-Lilly is prepared from liver extract-Lilly. One batch of this powder is dissolved in water, the solution is filtered and 0.5 per cent phenol is added as a preservative. Another batch of the powder is treated with ammonium sulfate and alcohol to remove much of the total solids. This more highly potent material is then also made up in the form of a water solution, and 0.5 per cent phenol is added. The two different solutions thus obtained from separate batches of the powder are then mixed to obtain a solution with a potency of 2 U. S. P. injectable units per cubic centimeter. Products of lower potency are prepared by adding water to the final product.

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SATURDAY, MAY 31, 1941

TRAUMA AND STRAIN IN RELATION TO POLIOMYELITIS

The widespread dissemination of the virus of poliomyelitis, when contrasted with the relatively limited incidence of the disease, suggests the existence of a number of contributing causative factors besides the virus. Isolated reports of the effects of either trauma or strain as predisposing factors in the development of acute anterior poliomyelitis are not infrequent. Frey [1] reported two cases following fractures in children 3 years old and one in a girl of 14 following the removal of a small chondroma from the left humerus. The disease developed within one month, two and one-half months and one and three-fourths months, respectively. The flaccid paralysis in each case corresponded to the seat of the trauma and to the same spinal cord segment. Zenke [2] reported three cases following trauma. The flaccid paralysis in her cases likewise involved muscle groups corresponding to the spinal cord segments originally involved in the trauma. Both authors believe that functional damage to the corresponding segment of the anterior horn ganglion cells acted as the predisposing factor. Bodily overexertion has recently been accorded particular attention as a possible predisposing cause. Thus, Voss [3] reported the case of a girl aged 17 years who contracted acute anterior poliomyelitis of the Landry type after a strenuous tennis match. Bremer [4] reported the case of a student in whom the disease developed following a difficult mountain climb. The observations of de Rudder and Petersen [5] are particularly instructive in this connection. These authors describe two small epidemics which broke out abruptly after an athletic contest, in a boarding school located in a small rural community in southern Germany. The boys were of the ages between 13 and 19, in the best of health and trained in athletics. Within a week after the athletic contest eleven boys came down with the disease. Another group of six boys came down with the disease following the second athletic contest a few days later. Three boys who attended the contest but did not participate in the games also developed the disease, bringing the total to twenty. Of these, 14 were abortive cases while 6 were complicated by paralyses. There were no other cases in that territory and none developed in the course of the following year. The total number of the boys in this school amounted to one hundred and seven; thus the morbidity was 20.5 per cent, which is much higher than any incidence thus far reported for any community.

Nase [6] reported the case of a 26 year old soldier who, in the course of exercises, fell and struck his occiput and back. The accident was not followed by any alarming symptoms, so that the next day he was able to participate in a cross-country run, at the completion of which he appeared completely exhausted. There developed vomiting and rapid rise of temperature. On admission to the hospital the following morning he was not able to sit up in bed, to turn or to move his limbs except with difficulty. There was a moderate spasm of the right arm and some spasticity on bending the neck forward. His breathing was difficult. Death took place from respiratory paralysis nine hours after admission. The necropsy revealed no injury to the brain or the spinal cord. Microscopic examination revealed characteristic perivascular infiltration, lymphocytic and leukocytic infiltration, and destruction of the ganglionic cells of the anterior horns, most pronounced in the cervical segment of the spinal cord but also present in the medulla oblongata and in the white substance. The pathologist's diagnosis was acute anterior poliomyelitis. The presence of the patellar and abdominal reflexes, the spasticity of the right arm and the absence of flaccid paralyses constitute an atypical picture. However, Foerster and other writers have described atypical forms of acute anterior poliomyelitis in which increased reflexes and spasticity of certain muscle groups were associated with flaccid paralysis of some of the extremities. Such clinical pictures were seen in the fulminant cases and were the result of ascending degeneration of the pyramidal tracts. Wickmann, in his studies of the epidemics of 1911 to 1913 in Sweden, described four main clinical types: (1) the spinal, (2) the encephalitic, (3) the meningitic and (4) Landry's paralysis. Nase's case presents a combination of the encephalitic, the meningitic and the Landry type.

Recent experimental work throws additional light on the influence of chilling and overexertion on the development of poliomyelitis. Sabin [7] has demonstrated that rhesus monkeys inoculated with the human virus may

1. Frey, Walter: Epidemische Kinderlähmung und Trauma, Schweiz. med. Wchnschr. **68:** 491 (April 30) 1938.
2. Zenke, Ursula: Poliomyelitis und Trauma, München. med. Wchnschr. **86:** 1153 (July 28) 1939.
3. Voss, G.: Ein Fall von Poliomyelitis ascendens acutissima, Deutsche med. Wchnschr. **58:** 1882 (Nov. 25) 1932.
4. Bremer, F. W.: Ueber das klinische Bild und die Therapie der Heine-Medinschen Krankheit beim Erwachsenen, Deutsches Arch. f. klin. Med. **173:** 58 (April 20) 1932.
5. de Rudder, B., and Petersen, G. A.: Steigert körperliche Anstrengung die Disposition zu epidemischer Kinderlähme? (Eine epidemiologische Beobachtung), Klin. Wchnschr. **17:** 699 (May 14) 1938.
6. Nase, H.: Poliomyelitis acuta anterior und Wehrdienstbeschädigung, München. med. Wchnschr. **88:** 293 (March 14) 1941.
7. Sabin, A. B.: Progress Report to the National Foundation for Infantile Paralysis.

develop a nonparalytic or even inapparent form of poliomyelitis with typical neuronal and infiltrative lesions in the spinal cord. He further found that the virus may actually reach the lower motor areas without paralysis necessarily ensuing, provided the proper equilibrium between the host and the virus exists or is achieved before too many nerve cells are affected. These observations have led to the consideration of assigning a new role to heavy exercise in the development of paralysis. The history of heavy exercise is frequently given by patients. Sabin found that the interval between this exercise and the onset of paralysis is usually less than twenty-four hours. This short interval, Sabin believes, suggests not only that those persons were already harboring the virus in their nervous system but also that it might already have involved their medulla and spinal cord and that the exercise could be the factor which converts what might have remained an unapparent or nonparalytic type of poliomyelitis into the frankly paralytic type of the disease.

Levinson [8] demonstrated that monkeys immersed in cold water and compelled to swim to the point of exhaustion developed more severe paralysis than did either those which remained in their cages or those which were immersed in water at body temperature and protected from exercise and chilling.

The subject of body strain deserves particular attention in connection with military service.

THE SIGNIFICANCE OF MORTALITY STATISTICS

In a carefully documented discussion on mortality statistics, Van Buren [1] points out a number of deductions which cannot be proved by such data. Entirely too much importance and finality, he says, are attached to many crude death rates. Thus, if calculations from the crude death rates for cancer over the twenty-five year period 1911-1935 are made, one would conclude that the mortality rate had increased over 41 per cent in the last year of the time series as compared with the first year. When corrected, however, for the effect of the changing age distribution, it develops that the increase was only 14.5 per cent—an entirely different picture.

Another common mistake in interpretation of mortality figures is the utter disregard of the fact that data for the expanding death registration area do not relate to the entire country for years prior to 1933. An example of the dangers inherent in failure to recognize this fact is cited by Van Buren: A news bureau recently gave to the press a statement that deaths from a certain cause had increased in the United States from 8,959 in 1920 to 19,802 in 1938 and had therefore more than doubled. The 1920 figure, however, related to only thirty-four states, the District of Columbia and sixteen cities in nonregistration states. The actual death rate was 10.2 per hundred thousand from this cause in 1920 and 15.2 in 1938. Obviously, the rate did not "more than double."

Similar difficulties in interpreting mortality statistics may be encountered merely because of change in classification under the International List of Causes of Death or may even be due to "fashion." Thus the rate for simple meningitis dropped continuously from 27.6 per hundred thousand in 1901 to 19.2 in 1905, while, at the same time, that for epidemic cerebrospinal meningitis rose from 5.7 to 15.0. The explanation, of course, is that there was constantly increasing care exercised by physicians to define "meningitis" as of the epidemic type. Similarly, the rate for diseases of the arteries almost doubled in these five years, owing largely to the growing practice of certifying "arteriosclerosis" instead of "old age," which latter, in turn, registered a continuously declining death rate.

Changing terms in the International List have resulted in many apparent alterations in the mortality data which do not, in fact, reflect the true picture. Thus, "endocarditis and myocarditis, unqualified, for ages 45 to 59" were transferred from the "acute endocarditis and myocarditis" title to the "other diseases of the heart" title. Since the proportion of the population in the 45 to 59 age group is steadily becoming larger, and since the terms endocarditis and myocarditis are often reported without qualification on the death certificates, these transfers assume considerable importance in their effect on the published death rates. Acute and chronic bronchitis can be cited as another title that presents difficulties with respect to comparability. The 1921 revision of the International List resulted in the transfer of the terms capillary bronchitis, cyst of bronchi and asthmatic catarrh from this rubric, while plastic bronchitis was added to it.

A classic example of misleading inferences from a time series of death rates is apparent in diseases of the coronary arteries. Death rates are available beginning with 1930, when deaths from coronary diseases were first segregated in the mortality statistics. If the figures are accepted at their face value, an astounding situation is revealed: one must conclude that in the short period of eight years the rate for this cause of death increased continuously from 8.0 per hundred thousand in 1930 to 52.0 in 1938. This abrupt rise is, of course, largely spurious. In the first place, diagnostic skill in relation to coronary diseases improved during the decade, but the chief factor in the apparent sharp increase was the growing "fashion" among physicians when clinical diagnosis was undertaken in cardiac cases to report the death as coronary occlusion, coronary thrombosis or coronary sclerosis. Thousands of deaths which prior to 1930 would have been allocated to other rubrics relating to diseases of the heart have been assigned, since 1930,

8. Levinson, S. O.: Progress Report to the National Foundation for Infantile Paralysis.
1. Van Buren, G. H.: Some Things You Can't Prove by Mortality Statistics.

to coronary disease. Factors such as Van Buren cites should lead toward the employment of extraordinary caution in the interpretation of comparative mortality statistics.

Current Comment

HYPOTHYROIDISM IN CHILDREN

Physicians often have difficulty in diagnosing hypothyroidism in children. One of the commonest errors is to think that mongolian idiots are cretins. Many times mongolian idiots referred by practicing physicians to children's clinics arrive with the diagnosis of cretinism. Mentally defective children are often considered to be cretins solely because of their retarded mental development and particularly if they happen to have a puzzled expression and queer physiognomy. Dwarfism, even if not accompanied by any of the stigmas of hypothyroidism, is often thought to depend on deficiency of the thyroid, probably because hypothyroidism is so well known as a cause of dwarfism. An error which has become common recently is to consider delay in the development of the centers of ossification of the epiphyses as being due to hypothyroidism. This is the outgrowth of the mistaken idea that the thyroid alone governs the maturation of the centers of ossification of the skeleton. The principal difficulty is that the physician is inclined to base the diagnosis of deficiency of thyroid on the finding of one or two suggestive signs. The paper of Wilkins and Fleischmann [1] which appears in this issue of THE JOURNAL is timely. It indicates the necessity of considering the entire clinical picture from the point of view of both functional and structural changes. Attention is drawn also to the fact that the character and extent of structural changes depend on the time of life when the deficiency occurs and the length of time it remains untreated.

THE BRAIN AND CHOLESTEROL METABOLISM

Comparatively recently it has been established that male and female sex hormones and the vitamin D group are cholesterol derivatives. The capacity of cholesterol esters to change into liquid crystalline anisotropic fats and to be deposited in the various tissues determines the unique character of disturbances of the cholesterol metabolism in pathology and particularly in the diseases of the aorta and arteries of man. P. D. Gorizontov,[1] working in the First Moscow Medical Institute, produced aseptic meningoencephalitis in dogs by subdural injection into the brain of either turpentine or silver nitrate. The comparative study of the blood cholesterol of the afferent arteries of the brain and of the blood cholesterol level of the efferent vessels of the brain demonstrated the development of hypercholesteremia in the experimental animals, which could not be explained on the basis of mobilization of cholesterol from the lipid depots of the brain but which the author interprets as the result of the increase of cholesterol synthesis in the brain. Gorizontov correlated the various biochemical data obtained in his experiments with the morphologic alterations in the brain of his experimental animals and established the dependence of the blood cholesterol levels in his animals on the reactive processes on the part of the ectodermal neuroglia cells of the brain. This interesting and entirely new concept of the role of neuroglia in the cholesterol metabolism presents not only a theoretical but also a practical interest, since concepts in pathology thus far do not recognize humoral significance of the brain. In the light of the view advanced by the author, the role of neuroglia in cholesterol metabolism is that of a detoxifying process; toxic brain lesions themselves may be regarded as the result of disturbance of metabolic function of the neuroglia. Thus, hypercholesteremia as a result of hyperfunction of the neuroglia cells of ectodermal origin plays an important part in the lesions of internal organs, as for example in the development of atheromatosis of the aorta and of the arteries.

1. Wilkins, Lawson, and Fleischmann, Walter: The Diagnosis of Hypothyroidism in Childhood, this issue, p. 2459.

1. Gorizontov, P. D.: The Role of the Brain in Cholesterol Metabolism: Role of Neuroglia in Pathogenesis of Cholesterinemia (in Russian), Moscow, Izdanie Pervago Moskovskogo, Meditsinskogo Instituta, 1940.

PROPHYLACTIC MEASURES FOR SYPHILIS AND GONORRHEA

The medical profession and the public health agencies bear a heavy responsibility for the prevention of syphilis and gonorrhea, especially during the present period of military mobilization. Both chemical and mechanical methods of prophylaxis have been definitely proved efficacious and, if their use is widely understood and correctly applied, there should be a great diminution in the incidence of both diseases. A preliminary statement on this subject by a special joint committee appointed by the American Social Hygiene Association and the United States Public Health Service, headed by H. H. Hazen, has recently appeared.[1] Health education with regard to syphilis and gonorrhea should include simple frank and explicit directions as to chemical and mechanical prophylaxis and in addition involves obligation on the part of health authorities to provide the facilities through which the means recommended may be made available. The following recommendations are made:

1. Safest method:
   - A. Use a condom of standard type.
   - B. Thoroughly wash the genitals and adjacent parts with soap and water as soon as possible (the sooner the better, but within one hour at most) after removal of the condom.
2. In the absence of a condom:
   - A. Thoroughly wash with soap and hot water as already described.
   - B. After urination, inject 6 cc. of 2 per cent strong protein silver solution, or other efficient, nonirritating germicidal solution into the urethra and hold for five minutes.
   - C. Rub 33 per cent ointment of mild mercurous chloride (calomel ointment) into the genitals and adjacent parts.

The committee emphasizes the fact that these methods are not 100 per cent successful but are sufficiently successful to deserve widespread application.

1. Hazen, H. H., et al.: The Chemical and Mechanical Prevention of Syphilis and Gonorrhea, Venereal Disease Information 21:311 (Oct.) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

NEUROPSYCHIATRIC EXAMINATION OF APPLICANTS FOR VOLUNTARY ENLISTMENT AND SELECTEES FOR INDUCTION

Circular Letter No. 19

1. The Surgeon General desires that medical officers examining applicants for voluntary enlistment and selectees for induction be especially alert to detect all persons with deficiency, constitutional psychopathy, prepsychotic and postpsychotic personality or psychosis and other persons who later may disrupt discipline and morale, retard progressive military training, occupy hospital beds urgently needed for acutely ill patients and finally become an economic burden on the government.

2. The following information is intended solely as a practical guide, and neuropsychiatrists are enjoined to apply it with discretion and mature judgment in order not to reject applicants or selectees without adequate and positive diagnostic indications of their unsuitability for active service, since their unwarranted rejection not only would constitute an injustice to the persons concerned but would deprive the government of their service.

3. During the period from April 1, 1917 to Dec. 31, 1919 no less than 97,657 patients were admitted to hospitals for persons with neuropsychiatric diseases. The major subclassification grouped 8,731 as hospitalized for epilepsy, 8,028 for neurasthenia, 4,310 for neurocirculatory asthenia, 6,090 for hysteria, 5,146 for constitutional psychopathic states, 13,063 for mental deficiency, 6,249 for dementia praecox, 7,501 for psychoneuroses, 5,652 for other types of psychoses and the remainder for various neuropsychiatric disorders. The foregoing brief analysis indicates the necessity of careful neuropsychiatric study of all questionable applicants on their examination at recruiting or induction stations.

4. The soldier must be looked on as a fighting unit requiring certain limited and definite qualifications. Not all persons are adaptable to restrictions and inhibitions of personal desires and comforts, to deprivation of rest, food or shelter or to the extraordinary demands for prolonged physical and mental activity often imposed by active military service. It must be remembered that many persons with abnormal personality traits who are capable of satisfactory adult adjustment in civilian life, in which numerous avenues of escape are available, will be at a total loss to adjust themselves to a pattern which is more or less inflexible and, of necessity, delimited and circumscribed as to self expression. When thrown on their own meager resources of adaptation in a military environment, in contact with all kinds of personalities, some who are just able to adapt themselves to life under the most favorable conditions will not fit into the one iron mold which experience has taught is essential to military success.

5. Applicants who manifest any of the following personality deviations require special attention on the part of the psychiatric examiner: instability, seclusiveness, sulkiness, sluggishness, discontent, lonesomeness, depression, shyness, suspicion, overboisterousness, timidity, sleeplessness, lack of initiative and ambition, personal uncleanliness, stupidity, dulness, resentfulness to discipline, nocturnal incontinence, sleepwalking, recognized queerness, suicidal tendencies (bona fide or not) and homosexual proclivities.

6. A brief résumé of the more common neuropsychopathic conditions is as follows:

GROUP I. *Mental Defects and Deficiencies.*—These are manifested by a lack of general information concerning the native environment; inability to learn, to reason, to calculate, to plan, to construct, to compare weights, and so on; defect in judgment, foresight, language and output of effort; suggestibility; untidiness; lack of personal cleanliness; anatomic stigmas of degeneration, and muscular awkwardness. The history of the school life and the vocational career as well as the disciplinary report will assist materially; then the applicant should be classified according to psychometric standards.

Examiners should use extreme care and judgment in reporting their findings on the enlistment record, since these records are given to the registrants when they are rejected and become common knowledge in the community. Such terms as "imbecile" and "moron" will not be used, but an approximate psychometric scaling will be listed as the cause for rejection, such as "mental age, 8 years." Elaborate psychometric estimation is not necessary, and any accepted abbreviated method will suffice. Intelligence cannot be definitely estimated, and no infallible test is available. The results are all only approximations and must be evaluated only in conjunction with accompanying factors and circumstances.

Illiteracy per se is not to be classified as mental deficiency.

GROUP II. *Psychopathic Personality Disorders.*—Under this heading is placed an ill defined, more or less heterogeneous group of conditions in which the patients, although they do not suffer from a congenital defect in the intellectual sphere, manifest a definite defect in their ability to profit by experience. They are unable to proceed through life with any definite pattern of standardized activity. They are unable to respond in an adult social manner to the demands of honesty, truthfulness, decency and consideration of their associates. They are emotionally unstable and not to be depended on; they act impulsively, with poor judgment; they are always in difficulties, have many and various schemes without any logical basis, lack tenacity of purpose, are easily influenced and are often in conflict with the law. They do not take kindly to regimentation and are continually at variance with those who attempt to indoctrinate them in the essentials of military discipline. Such persons have a decided influence on their associates and on the morale of the organization, for they will not conform to organized authority, and they derive much satisfaction from cultivating insubordination in others. Frequently they make a favorable impression, are neat, talk well and are well mannered. However, under this veneer the real defect is evident by past irresponsiveness to social demands and lack of continuity of purpose. In this general group are to be placed many homosexual persons, grotesque and pathologic liars, vagabonds, inadequate and emotionally unstable persons, petty offenders, swindlers, kleptomaniacs, pyromaniacs, alcoholic persons and likewise those highly irritable and arrogant persons the so-called pseudoquerulents ("guardhouse lawyers"), who are forever critical of organized authority and imbued with feelings of abuse and lack of consideration by their fellows.

GROUP III. *Major Abnormalities of Mood.*—Major abnormalities of mood are shown by episodes of unreasonable elation or depression which tend to recur without obvious connection with events. Persons who are known to be so mercurial in their reactions that their judgment is seriously impaired during the upward or downward swing of their moods should be rejected. Registrants known to have received medical or nursing care because of morbid excitement or depression should be rejected.

GROUP IV. *Psychoneurotic Disorders.*—Psychoneurotic disorders present a more difficult diagnostic problem. The signs and symptoms fall more or less clearly into one of three major categories: the hysterical, physical signs and symptoms often so dramatic that they may seem fraudulent and do not follow anatomically understandable patterns; the morbidly anxious, various signs and symptoms of fear, and the obsessional, which include such varied conditions as hypochondriacal states (preoccupation with one's ill health); morbid fears (phobias), and rituals of action and thought which the patients feel compelled to carry out.

The examiner should look for hysterical stigmas, such as cutaneous anesthesia (especially hemianesthesia); contractions of the visual fields, and so on; phobias; morbid doubts and fears; attacks of anxiety; compulsions, and hypochondriasis. He should compare the complaints with the behavior and obtain a history as to former nervous breakdowns and vocational career.

For purposes of classification, there are to be placed in this group the so-called psychosomatic disorders, mental or personality difficulties chiefly characterized by signs and symptoms of systemic disease—respiratory, gastrointestinal, cardiac, genitourinary or cutaneous. These include many examples of asthma, urticaria, "neurasthenic states," neurocirculatory asthenia, "effort syndrome," disordered action of the heart, paroxysmal tachycardia, gastric hyperacidity, pylorospasm, gastric and duodenal ulceration, spastic constipation and diarrhea, mucous colitis, impotence, urinary urgency or frequency and incontinence of semen. The examiner should look for a clear relation in the history of attacks coinciding with periods of personal stress and of improvement with separations from the accustomed stressful surroundings. These conditions sometimes appear early in the course of prepsychotic states discussed under group V.

GROUP V. *Conditions Associated with Dementia Praecox.*—This category comprises grave mental or personality handicaps. Persons with prepsychotic or postpsychotic personality and persons actually suffering from a schizophrenic ("dementia praecox") mental disorder manifest their condition by obscurely motivated peculiarities of behavior and thought. Of these, the so-called deteriorated states are the most obvious. Among such persons belong the numerous shiftless, untidy, perhaps morose, sometimes nomadic persons who have had what was regarded as a normal childhood. Somewhere between the ages of 12 and 25 they underwent a change, acute or insidious, with dilapidation of their social interests and the habits in which they had been trained. They may or may not have received treatment in hospitals for mental diseases.

Paranoiac personality traits comprise another large division. Paranoid persons cling to fantastic beliefs in their overwhelming importance and often feel that others are persecuting them or otherwise interfering with their career or their well being. Some of them believe that they are in communion with supernatural beings. Others believe that they are victims of plots, secret organizations, spy rings or religious or fraternal groups. They are often plausible in supporting these delusions by clever misinterpretation of facts. Some of them are evasive and skilful at concealing their disorder. A morbid suspiciousness of any one who takes an interest in them is frequent. They may become tense and hateful when interrogated. An attitude of unusual cautiousness or suspiciousness toward the examining physician or toward fellow registrants should suggest the possibility of paranoia.

The catatonic and prepsychotic states may present great difficulty in diagnosis. Perhaps the only obvious sign of these conditions is the impression of queerness. The actual oddities of behavior or thought may be subtle; it may be difficult in retrospect to point to any particular instances of the unusual. The most striking signs of these conditions may, in fact, come out in connection with the physical examination. The physician at some stage of the physical examination may observe a peculiar reaction which on questioning may awaken a suspicion of a prepsychotic state. Prepsychotic persons frequently entertain unfounded convictions as to bodily peculiarities or disorders which they attribute to excessive sexual acts of one sort or another. These beliefs, sometimes hard to elicit, are often medically incredible and bizarre. Questioning such persons on intimate personal matters often leads to great embarrassment, confused speech or actual blocking of thought, so that they do not know what to say.

Salient Deviations: These are indifference; apathy; withdrawal from the environment; ideas of reference and persecution; feelings of the mind being tampered with or of the thoughts being controlled by hypnotic, spiritualistic or other mysterious agencies; hallucinations of hearing; bodily hallucinations, frequently electrical or sexual; meaningless smiles, and, in general, inappropriate emotional reactions and a lack of connectedness in conversation. There may be sudden emotional or motor outbursts. The examiner should get the history of the family life and of the school, vocational and personal career.

GROUP VI. *Conditions Due to Chronic Inebriety.*—As evidences of alcoholism, one should look for suffused eyes; prominent superficial blood vessels of the nose and cheek; a flabby, bloated face; red or pale purplish discoloration of the mucous membrane of the pharynx and the soft palate; muscular tremor in the protruded tongue and extended fingers; tremulous handwriting; emotionalism; prevarication; suspicion; auditory or visual hallucination, and persecutory ideas. Early inebriety, especially in young selectees with morbid addiction to alcohol, may show no objective signs. A verified history of frequent breach of the law when drunk or of hospital treatment on account of alcoholism should be regarded as disqualifying.

For drug addiction one should look for pallor and dryness of the skin. If the drug is being used, the attitude is that of flippancy and mild exhilaration; if the drug has been withdrawn, it is cowardly and cringing. During the period of withdrawal there are also restlessness, anxiety and complaints of weakness, nausea and pains in the stomach, back and legs. There is distortion of the alae nasi. The pupils are contracted by morphine and dilated by cocaine. All habitual drug takers are liars. They do not drink, as a rule, and are inactive sexually. Many drug takers use needles and show white scars on the thighs, arms and trunk. Diacetylmorphine (heroin) addicts are mostly young men from the cities, often gangsters. They have a characteristic vocabulary and will talk much more freely about the habit if the examiner in his inquiries uses such words as "deck," "quill," "package," "an eighth," "blowers" and "cokie." A verified history of arrest for violation of the narcotic law should be regarded as disqualifying.

GROUP VII. *Conditions Accompanying Syphilis of the Central Nervous System.*—One should look for anomalous reaction of the pupil, facial tremor, speech defect in test phrases and in slurring and distortion of words in conversations and writing defects consisting of omissions and distortions of words. The mood is apathetic, depressed or euphoric. There are loss of memory and discrepancies in relating the facts of life. The knee jerks may be plus, minus or normal.

GROUP VIII. *Other Organic Diseases of Brain, Spinal Cord or Peripheral Nerves.*—Certain after-effects of organic nervous disease need not be causes for rejection provided (1) the disease is no longer operative and is not likely to recur and (2) the effect left by it does not prevent a satisfactory fulfilment of military duties. Examples of such conditions are paralysis of a few unimportant muscles following poliomyelitis; slight unilateral hypertonicity resulting from infantile hemiplegia in a man now robust, and various traumatic conditions. A history of hemiplegia occurring after infancy should always disqualify, even if no symptoms remain.

V 19

Existent organic nervous disease should always disqualify for military service. For example, neuritis of one or many nerves, while capable of recovery without resultant defect, is none the less a cause for rejection as long as it exists. The following organic nervous diseases are mentioned specifically, as they are the ones which frequently present few symptoms and may pass undetected by even the most skilful examiners:

Multiple Sclerosis: The symptoms are intention tremor, nystagmus, absence of abdominal reflexes and increased tendon reflexes. The scanning speech may be mistaken for stammering. There is no history of pain, but sometimes there is a history of urinary disturbance.

Progressive Muscular Atrophies and Dystrophies and Syringomyelia: One should look for atrophies in the small muscles of the hand and in the muscles of the shoulder girdle, with fibrillary twitchings. These plus anesthesia for heat and cold (scars on the hands from cuts and burnings) suggest syringomyelia. The history usually furnishes few data, although reference may be made to awkwardness. There is no history of pain. Syphilitic spinal disease imitates these conditions closely.

Epilepsies: There may be deep scars on the tongue, face and head. The voice is frequently characteristic. If one has the history alone, which may include incidents called faintness, dizziness or spasms of the face or of an extremity, one should verify by correspondence with physicians if practicable.

Hyperthyroidism: This is a nervous disease in its effects. There are persistent tachycardia, exophthalmos, tremor and an enlarged thyroid. There is a history of general nervousness.

7. In addition to the foregoing conditions, there are certain groups of symptoms which should be carefully investigated. They may not by themselves be sufficient for an exact diagnosis, but they generally indicate that the nervous system is seriously diseased and totally undependable for any continuous service.

General Symptoms.—These include abnormal attitudes, postures, contractions, contractures, deformities, atrophies or hypertrophies, marked kyphosis, scoliosis or lordosis, vasomotor or trophic disturbances, abnormal bodily and facial distribution of hair and abnormal distribution of fat.

Station and Gait.—A spastic gait, a scissors gait, marche à petits pas, cerebellar ataxia, a grotesque, histrionic or dancing gait, steppage, waddling, a bizarre gait, a nondescript gait (as seen in hysterical conditions), festination, propulsion, retropulsion, lateropulsion or loss or diminution of the normal automatic associated finer movements in walking may be observed.

Abnormal Coordination.—This is shown by the Romberg sign, cerebral and cerebellar ataxia, nonequilibratory ataxia, dysmetria and adiadokokinesis.

Abnormal Motility.—There may be abnormal motility of the eyes, face, mouth, neck or large joints.

Abnormal Involuntary or Spontaneous Movements.—Tremors, intentional or otherwise, nystagmus, fibrillation, choreic movements, athetosis or spasm may be noted.

Abnormal Reflexes.—Various reflex abnormalities may be present throughout the body (Babinski, Oppenheim, Gordon or Chaddock sign; grasping and groping reflexes; ankle clonus).

Sensory Abnormalities.—There may be hypesthesia, hyperesthesia, paresthesia, analgesia, thermesthesia, altered vibratory, joint, tendon or position sense, defective localization or defective stereognosis.

Evidence of Pathologic Change in Cranial Nerves.—This includes areas of tenderness over the calvarium and postencephalitic and posttraumatic syndromes.

8. The Army is one of the elements of national defense, and its present mission is one of preparation for an offensive-defensive type of warfare. It is in no sense a social service or a curative agency. It is to be considered neither a haven of rest for wanderers nor a corrective school for misfits, ne'er-do-wells, feebleminded persons or chronic offenders. Furthermore, it is neither a gymnasium for the training and development of the undernourished or undeveloped nor a psychiatric clinic for proper adjustment to adult emotional development. Therefore, there is no place within the Army for physical or mental weaklings, potentially psychotic or prepsychotic persons or behavior problems. Men who present behavior problems in the civilian community will certainly present intensified problems in the service.

9. While the aforementioned facts are brought to the examiner's attention, he is enjoined to interpret them not as a basis for lightly rejecting men for military service but rather as points on which to evaluate them with a view to eliminating the unfit and retaining those capable of satisfactorily performing the duties of soldiers.

THE NATIONAL YOUTH ADMINISTRATION HEALTH PROGRAM

While about 80 per cent of the young people employed by the National Youth Administration are fit for any type of work, nine out of every ten have health defects, most of which can be remedied provided suitable treatment is made available, according to preliminary statistics compiled under the health program of the National Youth Administration.

These figures are based on the results of medical examinations of ten thousand NYA workers made by local practicing doctors and dentists who have been employed by the National Youth Administration to do this work. The records tabulated to date reflect the health needs of youth as seen by physicians from twenty-one states representing all geographic regions of the United States.

With the cooperation of the medical profession as well as of federal and state health authorities, the National Youth Administration's health program[1] now operates in all states. The basis of this health program, which is an important part of the defense work of this agency, is a medical examination which facilitates assignment of youth to suitable work activities and at the same time discloses to young people their need for remedial treatment.

While the primary aim of the NYA is to provide young people with basic work experience to fit them for jobs in private industry, it has a logical concern with building up the health and physical fitness of its employees, both from the standpoint of the national welfare and as the largest employer of youth labor in the country.

HEALTH STATUS CLASSIFICATION

Young people who have been given health examinations have been grouped into health status classifications according to their physical ability to work and to engage in athletic activity. While six groupings are actually being used, these will be condensed here into four:

Group A comprises 78 per cent of all youth examined. It represents those who are at present fit for any type of employment or athletic activity. The individuals of this group, although fit for any employment, received one hundred and thirty health recommendations for each hundred youths. The rate for females was considerably higher than for males.

Group B comprises 13 per cent of all youth examined. It represents those who have defects not thought to be amenable to correction but not severely handicapping. There were one hundred and sixty health recommendations for each hundred youths in this group.

Group C comprises 5.5 per cent of all youth examined. It represents those whose assignment to a particular job should be approved by a physician. Some require medical supervision on the job. There were two hundred and ten health recommendations for each hundred youths in group C.

1. The National Youth Administration Contributes to the National Health, J. A. M. A. 115:2185 (Dec. 21) 1940.

Group D comprises 2.5 per cent of those examined. It represents those who are temporarily or permanently unfit for any employment. There were two hundred and ninety health recommendations for each hundred youths.

RECOMMENDATIONS, TYPE AND AMOUNT

Dental care was recommended for 56 per cent of those examined. This is made up of recommendations made by both physicians and dentists. If dentists had been used to make the dental examination for each youth, the figure would have been considerably higher, since among youth examined by dentists 72 per cent were reported as having carious teeth, while physicians reported only 47 per cent.

It is of interest that, in 10 per cent of the youth, each had from ten to thirty decayed teeth.

Tonsillectomy was recommended for 15 per cent.

Refraction was recommended for 15 per cent.

Special diets were recommended for 10 per cent.

Minor surgery, including hemorrhoidectomies and circumcisions, was recommended for 6 per cent.

Venereal disease treatment was recommended for 2 per cent. If a youth is already under treatment for a venereal disease, many physicians do not recommend treatment in this type of examination, although they do note presence of the disease.

Major surgery, including hernia repair, was recommended for 2 per cent.

Hookworm treatment was recommended for 2 per cent. Considering youth from the Southern states only, treatment for hookworm disease and hookworm infection was recommended for 5 per cent.

OTHER FINDINGS

Slightly over 5 per cent were described as being malnourished, while obesity was present in 3 per cent.

Organic heart disease was reported in almost 3 per cent of those examined.

In this first group to be reported, tuberculin testing and chest roentgenograms had not been completed; however, the finding of 95 cases of pulmonary tuberculosis were reported, of which 26 were active.

One of the most significant results of these examinations as far as the medical profession is concerned is the revelation that 25 per cent of the youths examined reported they had never been to a dentist and 18 per cent reported that they had never been to a physician. This disclosure is especially meaningful when one remembers that this is a group of young people who have been out of our public schools only a short time and presents a real challenge to those interested in health education and the application of preventive medicine.

The eight leading health defects for which corrections have been recommended can largely be taken care of in clinics or offices of physicians and dentists. Only a small group need hospitalization. Most of the health defects noted do not affect, at this early age, the ability of approximately 80 per cent of these youths to work, but many of the defects will influence unfavorably the selection of many youths by private industry and will, at a slightly later stage in life, decidedly affect the efficiency of the individual on any job, as well as eligibility for military service.

One of the main contributions of the NYA in obtaining treatment for young people who need it has been the payment of a wage to its youth employees which has enabled many to pay the cost of medical and dental care. NYA has placed many young people in contact with practicing physicians and dentists and has encouraged special private arrangements between the youth and the physician for defraying the cost of professional services. Where public or private clinics exist, it has been possible to facilitate access to these agencies for a sizable group of young people.

On the basis of experience thus far, it is believed that about 50 per cent of the NYA youth can be provided with needed health service through some such arrangements, depending on geographic locations. The remaining group of youth present a problem for which there is no present solution.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

WAR DEPARTMENT

The following additional medical reserve corps officers have been ordered to extended active duty by the War Department, Washington, D. C.:

ANDERSON, Milford Xerxes, 1st Lieut., Los Angeles.
ARNESON, Charles Albert, Captain, Fargo, N. D.
AXELROD, Harold, 1st Lieut., Brooklyn.
BAKER, Norman Ludlow, 1st Lieut., Chicago.
BALL, George Lindsay, Captain, Washington, D. C.
BARRETT, Richard Henry, 1st Lieut., Rochester, Minn.
BARTLETT, Walter Merritt, 1st Lieut., Benton Harbor, Mich.
BEEKINK, Ernest Henry, Captain, Grand Haven, Mich.
BERMAN, Leonard Stanley, 1st Lieut., Washington, D. C.
BISHOP, Harold Francis, 1st Lieut., Valhalla, N. Y.
BOSS, Myron Theodore, 1st Lieut., Baltimore.
BROWN, Charles Howard, 1st Lieut., Beverly Hills, Calif.
BURFORD, Edgar Humber, Captain, St. Louis.
BURRAGE, William Champlin, 1st Lieut., Boston.
CHALLMAN, Samuel Alan, Captain, Minneapolis.
DAVIS, Fenimore Edison, Captain, Ann Arbor, Mich.
DELEHANTY, John Thomas, 1st Lieut., Lattimer, Luzerne County, Pa.
FIENBERG, Robert A., 1st Lieut., Westfield, Mass.
FISHER, Roy Lee, Captain, Frederick, Okla.
FRENCH, Adam James, 1st Lieut., Ann Arbor, Mich.
GOLDBERG, Solomon, Captain, Pittsburgh.
HARWELL, Carl Mallory, Jr., 1st Lieut., Memphis, Tenn.
ISLER, Nathaniel Charles, Captain, Jeffersonville, Ind.
KING, Albert Terrence, 1st Lieut., Salem, Ore.
KREFT, Alfred John, 1st Lieut., Des Plaines, Ill.
KROTCHER, Lester Clayton, Captain, Twin Falls, Idaho.
LEA, Joseph Davis, 1st Lieut., New Orleans.
LEFFINGWELL, Forrest Emmett, Captain, Montebello, Calif.
McLOUGHLIN, Christopher John, 1st Lieut., Rochester, Minn.
MALTRY, Emile, Jr., 1st Lieut., New Orleans.
MILLER, Samuel Lewis, Captain, Cheboygan, Mich.
NACHTMAN, Howard Frank, 1st Lieut., Portland, Ore.
NEIBRIEF, Milton Nelson, 1st Lieut., Brooklyn.
NOONAN, Thomas Robert, 1st Lieut., Rochester, N. Y.
PLUM, John Bernard, 1st Lieut., Grand Rapids, Mich.
POWERS, Pierce William, 1st Lieut., St. Louis.
REEVES, David Lander, Captain, Los Angeles.
RICE, Dale Arthur, 1st Lieut., Meadville, Pa.
SEID, Sidney E., Captain, Chilocco, Okla.
SMITH, Eugene, 1st Lieut., Waterloo, Iowa.
SPENCER, Newton Carman, Major, Toledo, Ohio.
STADLER, Harold Erwin, 1st Lieut., Iowa City.
SUGAR, Samuel Jacob Nathan, 1st Lieut., Washington, D. C.
TANNER, Henry Seiver, 1st Lieut., Indianapolis.
THATCHER, Donald Sheldon, 1st Lieut., Milwaukee.
WHITEHEAD, Duncan, Captain, Leominster, Mass.
WOLPAW, Sidney Elmer, 1st Lieut., Cleveland Heights, Ohio.
YOUNG, John D., Jr., 1st Lieut., Lexington, Ky.

FIRST CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, First Corps Area, which comprises the states of Maine, Vermont, New Hampshire, Massachusetts, Rhode Island and Connecticut:

ALLEN, Howard H., 1st Lieut., Greensboro, Vt., Fort Devens, Mass.
ANDERSON, Donald L., 1st Lieut., Caribou, Maine, Fort Devens, Mass.
ANDERSON, Fred A., 1st Lieut., West Roxbury, Mass., Fort Devens, Mass.
ANTOS, Chester J., 1st Lieut., Salem, Mass., Fort Devens, Mass.
ARCHAMBAULT, Rene F., Captain, Barre, Vt., Fort Devens, Mass.
BARD, Henry H., Captain, Pittsfield, Mass., Camp Edwards, Mass.
BARRETT, Charles G., Captain, Amherst, Mass., Fort Devens, Mass.
BOTTAMINI, Joseph T., 1st Lieut., Burlington, Vt., Fort Devens, Mass.
BROWE, John H., 1st Lieut., Hartford, Conn., Fort Williams, Maine.
BURGIN, Leo B., Captain, Brookline, Mass., Fort Devens, Mass.
BUTTLES, Roy V., 1st Lieut., Burlington, Vt., Fort Devens, Mass.
CAHILL, Francis P., 1st Lieut., Cambridge, Mass., Manchester, N. H.
CAMPBELL, Kenneth D., 1st Lieut., Somerville, Mass., Manchester, N. H.
CASE, Edward P., Lieut. Col., West Hartford, Conn., Fort Adams, R. I.
CHOATE, Paul M., 1st Lieut., West Barnet, Vt., Fort Devens, Mass.
CLARK, Benjamin F., Captain, St. Johnsbury, Vt., Fort Devens, Mass.
CLEMENT, Howard R., 1st Lieut., Boston, Camp Edwards, Mass.
CURTIS, Sprague, 1st Lieut., Westfield, Mass., Fort Devens, Mass.
DENNING, Walter S., 1st Lieut., Brookline, Mass., Fort Devens, Mass.
DeWITT, Reginald F., 1st Lieut., Plymouth, N. H., Fort Devens, Mass.
EASTMAN, Cyrus D., 1st Lieut., Monroe, N. H., Fort Devens, Mass.

ESTABROOK, John S., 2d Lieut., Brandon, Vt., Fort Devens, Mass.
FINKS, Henry, 1st Lieut., Portland, Maine, Bangor, Maine.
FROMER, John L., Captain, Brookline, Mass., Fort Devens, Mass.
GALLERY, Daniel F., 1st Lieut., Fall River, Mass., Manchester, N. H.
GENCARELLI, Alphonse F., 1st Lieut., Hartford, Conn., Fort Devens, Mass.
GINGOLD, Thomas L., Major, New Haven, Conn., Fort Banks, Mass.
GLADSTONE, Arthur, 1st Lieut., Burlington, Vt., Bangor, Maine.
GODDARD, Philip A., 1st Lieut., Morrisville, Vt., Bangor, Maine.
GOERGEN, William P., 1st Lieut., Danbury, Conn., Bangor, Maine.
GOLDSBERRY, John J., 1st Lieut., Worcester, Mass., Fort Dix, N. J.
GOODRICH, William, 1st Lieut., Bridgeport, Conn., Fort Devens, Mass.
HAMMER, Joseph, 1st Lieut., Wellesley, Mass., Bangor, Maine.
HARWOOD, Clarence W., 1st Lieut., Burlington, Vt., Fort Devens, Mass.
HARWOOD, Clifford B., 1st Lieut., Whitingham, Vt., Fort Devens, Mass.
HERSEY, Thomas F., 1st Lieut., Hamden, Conn., Fort Devens, Mass.
HOBBS, Milford L., 1st Lieut., Burlington, Vt., Camp Edwards, Mass.
ISENSTEIN, Charles, 1st Lieut., Dorchester, Mass., Camp Edwards, Mass.
JORESS, Mark H., 1st Lieut., Lynn, Mass., Camp Edwards, Mass.
LAKE, Fredric D., 1st Lieut., Springfield, Mass., Fort Devens, Mass.
LEVIN, Harold M., 1st Lieut., Burlington, Vt., Bangor, Maine.
LEVIN, Spencer E., Captain, Roxbury, Mass., Fort Devens, Mass.
LEVINE, David I., 1st Lieut., Weymouth, Mass., Camp Edwards, Mass.
MAHONEY, James P., 1st Lieut., Burlington, Vt., Fort Devens, Mass.
MELLION, Jacob, Captain, New Britain, Conn., Camp Edwards, Mass.
MERRIAM, Philip G., 1st Lieut., New Britain, Conn., Fort Devens, Mass.
MILLSTEIN, Hyman, 1st Lieut., Southwest Harbor, Maine, Fort Devens, Mass.
MONROE, Willys M., Major, Pittsfield, Mass., Camp Edwards, Mass.
MONTGOMERY, Eugene P., 1st Lieut., Boston, Camp Langdon, N. H.
PERLEY, John R., 1st Lieut., Lakeport, N. H., Fort Devens, Mass.
RABNOWITZ, Henry, 1st Lieut., Brockton, Mass., Camp Edwards, Mass.
RADCLIFFE, Ernest J., Captain, Amherst, Mass., Bangor, Maine.
SKELTON, Alton B., 1st Lieut., Winchendon, Mass., Camp Edwards, Mass.
SMITH, Joseph, Captain, Providence, R. I., Manchester, N. H.
TIMMERMAN, Frederick W., 1st Lieut., Morrisville, Vt., Fort Devens, Mass.
TUCKER, Arthur S., 1st Lieut., New Haven, Conn., Camp Edwards, Mass.
TUOHY, Edward L., 1st Lieut., Cambridge, Mass., Camp Edwards, Mass.
TWADELLE, Frank J., 1st Lieut., Wellesley, Mass., Camp Edwards, Mass.

FOURTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Fourth Corps Area, which comprises the states of Tennessee, North Carolina, South Carolina, Alabama, Georgia, Mississippi, Florida and Louisiana:

ANTONAKOS, Theodore, 1st Lieut., Winston-Salem, N. C., MacDill Field, Fla.
ASLING, Clarence W., 1st Lieut., Nashville, Tenn., Camp Croft, S. C.
AUERBACH, Stewart H., Captain, Augusta, Ga., Camp Wheeler, Ga.
BAILEY, Thomas E., 1st Lieut., Augusta, Ga., Camp Davis, N. C.
BANNS, John Adam, 1st Lieut., Birmingham, Ala., Fort Bragg, N. C.
BARKOFF, Samuel A., 1st Lieut., New Orleans, MacDill Field, Fla.
BASS, Beaty Lee, 1st Lieut., Winston-Salem, N. C., Fort Bragg, N. C.
BLAIR, Charles P., 1st Lieut., Coushatta, La., Camp Polk, La.
BLEECKER, Philip B., 1st Lieut., Memphis, Tenn., Fort Bragg, N. C.
BODDIE, James B., Jr., 1st Lieut., Nashville, Tenn., Fort Benning, Ga.
BOMBET, Charles N., 1st Lieut., Baton Rouge, La., Fort Benning, Ga.
BOSTWICK, Jackson L., 1st Lieut., Jacksonville, Fla., Fort Benning, Ga.
BOURKARD, Ernest Richard, 1st Lieut., Miami, Fla., Camp Davis, N. C.
BOWEN, Jack H., 1st Lieut., Jacksonville, Fla., Fort Bragg, N. C.
BRANNEN, Frank S., 1st Lieut., Chattanooga, Tenn., Fort Bragg, N. C.
BYRON, Robin Adair, 1st Lieut., New Orleans, Fort Bragg, N. C.
CASH, Ralph Louard, 1st Lieut., New Orleans, Fort Bragg, N. C.
CHAMBERS, John M., Jr., 1st Lieut., Memphis, Tenn., MacDill Field, Fla.
COOLEY, Beamon S., Jr., 1st Lieut., Birmingham, Ala., Fort Barrancas, Fla.
CROFT, Theodore C., 1st Lieut., Jacksonville, Fla., Camp Livingston, La.
DANIEL, Rollin A., Jr., Captain, Nashville, Tenn., Camp Forrest, Tenn.
DODSON, George D., Jr., 1st Lieut., Chattanooga, Tenn., Camp Croft, S. C.
DOWELL, James W., 1st Lieut., Pineville, La., Camp Croft, S. C.
DOZIER, Horace B., 1st Lieut., New Orleans, Camp Croft, S. C.
DURHAM, Bon M., 1st Lieut., Augusta, Ga., Camp Croft, S. C.
DYER, John Lewis, 1st Lieut., New Orleans, Camp Blanding, Fla.
ELLIOTT, Cecil B., 1st Lieut., Gainesville, Ga., Fort Bragg, N. C.
ELLIS, Frank P., Jr., 1st Lieut., Birmingham, Ala., Fort Bragg, N. C.
FARRAGUT, Loyall David, Captain, Jonesboro, Tenn., Camp Forrest, Tenn.
FARRAR, Taylor, 1st Lieut., Shelbyville, Tenn., Camp Forrest, Tenn.
FISHER, William G., 1st Lieut., New Orleans, Fort Bragg, N. C.
FITZGERALD, William J., 1st Lieut., New Orleans, Camp Davis, N. C.
FUNKE, Barclay, 1st Lieut., Alexandria, La., Camp Polk, La.
GRAY, Cyrus S., Jr., 1st Lieut., Durham, N. C., Camp Claiborne, La.
GREEN, Arthur W., 1st Lieut., Memphis, Tenn., Fort Bragg, N. C.
GREEN, Daniel M., 1st Lieut., Memphis, Tenn., Camp Blanding, Fla.
GREEN, James A., 1st Lieut., Atlanta, Ga., MacDill Field, Fla.
GREENBERG, S. A., 1st Lieut., Florence, S. C., Camp Polk, La.
GRIMES, William H., Jr., 1st Lieut., Colquitt, Ga., Fort Bragg, N. C.
HARRIS, Reuben Rhys, 1st Lieut., Birmingham, Ala., Camp Blanding, Fla.
HARVARD, Bell M., Jr., 1st Lieut., New Orleans, Fort Benning, Ga.
HASPEL, Robert B., 1st Lieut., New Orleans, Fort Benning, Ga.
HENDERSON, Hiliary H., Jr., 1st Lieut., Birmingham, Ala., Camp Livingston, La.
HENRY, Blondy S., 1st Lieut., Memphis, Tenn., Camp Davis, N. C.
HERBERT, William C., Jr., 1st Lieut., Spartanburg, S. C., Camp Forrest, Tenn.
HICKS, David Y., Jr., 1st Lieut., Augusta, Ga., Camp Wheeler, Ga.
HILL, Thurman K., 1st Lieut., Nashville, Tenn., Camp Livingston, La.
HILLARD, Irving R., 1st Lieut., Jackson, Tenn., Fort Bragg, N. C.
HOLLIMAN, Henry D., Jr., 1st Lieut., Atlanta, Ga., Fort Jackson, S. C.
HOLLOMAN, Walter G., 1st Lieut., Monroe, La., Camp Wheeler, Ga.
HOLMES, Verner S., 1st Lieut., McComb, Miss., Camp Forrest, Tenn.
HOLT, Benton B., Jr., 1st Lieut., Charleston, S. C., Fort Jackson, S. C.
HORN, Phillip Webster, 1st Lieut., New Orleans, Camp Blanding, Fla.
HUBBARD, George B., 1st Lieut., Nashville, Tenn., Camp Forrest, Tenn.
HUTTON, Vernon, Jr., 1st Lieut., Nashville, Tenn., Fort Jackson, S. C.
JACKSON, Truxton L., 1st Lieut., Nashville, Tenn., Fort Bragg, N. C.
JEANES, James Gregg, 1st Lieut., Clinton, S. C., Camp Davis, N. C.
JERNIGAN, Sterling H., 1st Lieut., Atlanta, Ga., Fort Benning, Ga.
KALMON, Edmond H., Jr., 1st Lieut., Nashville, Tenn., Camp Davis, N. C.
KELLY, Alex R., Jr., 1st Lieut., Augusta, Ga., Camp Davis, N. C.
KUNTZ, William M., 1st Lieut., New Orleans, Camp Claiborne, La.
LAMBETH, Samuel S., III, 1st Lieut., Durham, N. C., Fort Bragg, N. C.
LANE, Thomas H., 1st Lieut., Fairfield, Ala., Camp Livingston, La.
LEVIN, Harold B., 1st Lieut., Atlanta, Ga., Camp Blanding, Fla.
LEWIS, Lawrence C., Jr., 1st Lieut., Tuskegee, Ala., Camp Blanding, Fla.
LOVE, William G., Jr., 1st Lieut., Atlanta, Ga., Fort Benning, Ga.
LOWENSTEIN, Sol L., 1st Lieut., Nashville, Tenn., Camp Livingston, La.
LYLE, Philip Lewis, 1st Lieut., Clarksville, Tenn., Camp Polk, La.
MacPHERSON, Ford J. A., 1st Lieut., Iberlin, La., Camp Shelby, Miss.
McCOSH, Walter W., Jr., 1st Lieut., Shreveport, La., Fort Bragg, N. C.
MAGNE, Jacques A., 1st Lieut., New Orleans, Camp Polk, La.
MARTIN, George H., 1st Lieut., Anguilla, Miss., MacDill Field, Fla.
MASON, James M., III, 1st Lieut., Birmingham, Ala., Fort Bragg, N. C.
MASTERS, ELIAS W., 1st Lieut., Anderson, S. C., Fort Jackson, S. C.
MICKAL, Abe, 1st Lieut., New Orleans, Fort Bragg, N. C.
MILLER, John M., 1st Lieut., Augusta, Ga., Fort Bragg, N. C.
MITCHELL, Charles B., Major, Mississippi A. & M. College, Camp Shelby, Miss.
MITCHELL, George J., 1st Lieut., Meridian, Miss., Camp Blanding, Fla.
MONTAGNET, J. M., Jr., 1st Lieut., New Orleans, Camp Forrest, Tenn.
MORROW, Arch S., 1st Lieut., Jacksonville, Fla., Fort Bragg, N. C.
MOTTY, Jules Stall, 1st Lieut., New Orleans, Camp Davis, N. C.
MURPHY, Robert J., Jr., 1st Lieut., Durham, N. C., Fort Bragg, N. C.
NETTERVILLE, Rush E., 1st Lieut., New Orleans, Camp Croft, S. C.
NICHOLS, Ralph Gibbs, 1st Lieut., Knoxville, Tenn., Camp Polk, La.
NILES, George A., Jr., 1st Lieut., Atlanta, Ga., Camp Davis, N. C.
PARKS, Lorenzo Lynn, Major, Jacksonville, Fla., Headquarters 4th Army Corps, Jacksonville, Fla.
PARNELL, Homer S., Jr., 1st Lieut., New Orleans, Camp Polk, La.
PARROTT, John H., 1st Lieut., Camp Shelby, Miss., Fort Benning, Ga.
PASTERNACK, Morris, 1st Lieut., New Orleans, Fort Jackson, S. C.
PATTERSON, McLeod, 1st Lieut., New Orleans, Camp Croft, S. C.
PEPE, John Luke, 1st Lieut., New Orleans, Fort Jackson, S. C.
PETERSON, Bedford F., 1st Lieut., Bolivar, Tenn., Camp Wheeler, Ga.
PHILLIPS, Benjamin J., 1st Lieut., New Orleans, Fort Jackson, S. C.
PHILLIPS, James B., Jr., 1st Lieut., Chattanooga, Tenn., Camp Croft, S. C.
PINSON, Harry D., 1st Lieut., Augusta, Ga., Camp Croft, S. C.
PIZZOLATO, Philip, 1st Lieut., New Orleans, Camp Croft, S. C.
POLITES, Nicholas, 1st Lieut., Wilmington, N. C., Camp Polk, La.
POLLARD, Edward V., 1st Lieut., Parsons, Tenn., Fort Bragg, N. C.
POPE, Madison R., 1st Lieut., Charleston, S. C., Fort Bragg, N. C.
RAGGIO, Francis W., Jr., 1st Lieut., New Orleans, Camp Wheeler, Ga.
RAGSDALE, William E., Jr., 1st Lieut., Memphis, Tenn., MacDill Field, Fla.
RANCK, Edward Buford, 1st Lieut., Atlanta, Ga., Camp Forrest, Tenn.
RAVENEL, Joseph A., 1st Lieut., New Orleans, MacDill Field, Fla.
RAY, Russell B., 1st Lieut., Memphis, Tenn., MacDill Field, Fla.
RHAME, Delmar O., Jr., 1st Lieut., Clinton, S. C., Camp Livingston, La.
ROBINSON, Edward B., Jr., 1st Lieut., Birmingham, Ala., Camp Blanding, Fla.
SCHONLAU, James W., 1st Lieut., Shreveport, La., Camp Forrest, Tenn.
SILBERMAN, Donald J., 1st Lieut., Birmingham, Ala., Camp Claiborne, La.
SIMMONS, William G., 1st Lieut., Emory, Ga., MacDill Field, Fla.
SMERZNAK, John J., 1st Lieut., Concord, N. C., Camp Livingston, La.
SMITH, Harold M., 1st Lieut., Savannah, Ga., Camp Wheeler, Ga.
SPITZBERG, R. H., 1st Lieut., Mobile, Ala., Camp Forrest, Tenn.
STANDER, Alvin A., 1st Lieut., Baton Rouge, La., Camp Davis, N. C.
STELLING, Frank H., III, 1st Lieut., Augusta, Ga., Camp Croft, S. C.
STERN, Henry M., 1st Lieut., New Orleans, Camp Davis, N. C.
STEWART, James B., 1st Lieut., Milledgeville, Ga., Fort Benning, Ga.
STILLMAN, Sidney, 1st Lieut., New Orleans, Fort Bragg, N. C.
SUARES, John C., 1st Lieut., New Orleans, Camp Croft, S. C.
TALBOT, Joe Dudley, 1st Lieut., New Orleans, Fort Bragg, N. C.
TATUM, Roy Carroll, Lieut. Col., Salisbury, N. C., Med. Rep. 1st M. A., Knoxville, Tenn.
THOMAS, Henry W., 1st Lieut., Atlanta, Ga., Fort Bragg, N. C.
THOMAS, Herbert H., 1st Lieut., University, Ala., Fort Bragg, N. C.

THOMAS, Paul J., 1st Lieut., New Orleans, MacDill Field, Fla.
THOMPSON, Samuel B., 1st Lieut., Fairfield, Ala., Camp Polk, La.
TIMMERMAN, William B., 1st Lieut., Hartsville, S. C., Camp Wheeler, Ga.
VARINO, George A., 1st Lieut., Monroe, La., Camp Davis, N. C.
VARNER, John B., 1st Lieut., Memphis, Tenn., Fort Bragg, N. C.
VINSANT, Lowell E., 1st Lieut., Knoxville, Tenn., Fort Bragg, N. C.
VORDER BRUEGGE, Colin F., 1st Lieut., Memphis, Tenn., Camp Wheeler, Ga.
VUNK, Raymond H., 1st Lieut., Charleston, S. C., Fort Bragg, N. C.
WARD, Leamon M., 1st Lieut., New Orleans, Fort Bragg, N. C.
WEBB, George M., 1st Lieut., Tallulah, La., Camp Livingston, La.
WHITLEY, James R., 1st Lieut., Chattanooga, Tenn., MacDill Field, Fla.
WHITWORTH, Clyde W., 1st Lieut., Clarkesville, Ga., Camp Livingston, La.
WILKES, William A., 1st Lieut., Augusta, Ga., Fort Bragg, N. C.
WILLIAMS, Claiborne, 1st Lieut., Nashville, Tenn., Elementary Flying School, Tuscaloosa, Ala.
WILSON, Issac R., Jr., 1st Lieut., Charleston, S. C., Fort Bragg, N. C.
WILSON, James A., 1st Lieut., New Orleans, MacDill Field, Fla.
WILSON, John McQ., 1st Lieut., Memphis, Tenn., Camp Shelby, Miss.
WILSON, Shelburne D., 1st Lieut., Mountain City, Tenn., Fort Benning, Ga.
WYATT, Charles N., Captain, Greenville, S. C., Camp Forrest, Tenn.
YANCEY, Cyril T., 1st Lieut., New Orleans, Fort Bragg, N. C.
YOUNG, John D., 1st Lieut., Atlanta, Ga., MacDill Field, Fla.

SIXTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Sixth Corps Area, which comprises the states of Wisconsin, Illinois and Michigan:

ACOCKS, James R., 1st Lieut., Houghton, Mich., Selfridge Field, Mich.
ALBI, Raphael W., 1st Lieut., Lake City, Mich., Station Complement, Camp Wheeler, Ga.
ALBIN, Meyer S., 1st Lieut., Cadillac, Mich., Station Complement, Camp Wheeler, Macon, Ga.
ALLEGRETTI, Joseph E., Captain, Chicago, Station Complement, Camp Croft, S. C.
AXEL, Ben John, 1st Lieut., Madison, Wis., Station Complement, Fort Jackson, S. C.
BACHHUBER, Edward A., 1st Lieut., Mayville, Wis., Station Hospital, Fort Sill, Okla.
BENISON, Arthur L., 1st Lieut., Edmore, Mich., Station Complement, Camp Wheeler, Macon, Ga.
BERKELHAMER, Ralph C., 1st Lieut., Chicago, Station Complement, Camp Davis, N. C.
BUSCAGLIA, Chris J., 1st Lieut., Ypsilanti, Mich., 11th Station Hospital, Fort Custer, Mich.
BRAND, Ashley M., 1st Lieut., Chicago, 210th Corps Area (Antiaircraft), U. S. National Guard, Fort Sheridan, Ill.
BROOKS, Lewis C., Captain, Freeport, Ill., 27th Division, Fort McClellan, Ala.
BROWNELL, Paul G., 1st Lieut., Detroit, Station Complement, Fort Jackson, S. C.
CHRISTENSON, Albert W., Lieut. Col., Rockford, Ill., Savanna Ordnance Depot, Proving Ground, Ill.
CITRIN, Robert R., 1st Lieut., Peoria, Ill., 24th Infantry, Fort Benning, Ga.
CLAUDON, Dann B., 1st Lieut., Jefferson, Wis., Station Hospital, Camp Grant, Ill.
CLAXTON, Wilbert T., 1st Lieut., Britton, Mich., Station Hospital, Fort Sill, Okla.
DIETRICH, Hervey W., 1st Lieut., Madison, Wis., Medical Detachment, 7th Cavalry, Fort Bliss, Texas.
DUDLEY, Erwin F., Major, Decatur, Ill., 11th Station Hospital, Fort Custer, Mich.
DUNN, Marion F., 1st Lieut., Waukegan, Ill., Infirmary, Medical Replacement Center, Camp Grant, Ill.
EGGERS, John F., 1st Lieut., Sycamore, Ill., 27th Division, Fort McClellan, Ala.
ESPEY, Hugh S., 1st Lieut., Zenia, Ohio, Station Complement, Camp Croft, S. C.
FALICK, Mordecai L., 1st Lieut., Detroit, Station Complement, Fort Jackson, S. C.
FEIGELMAN, Meyer J., 1st Lieut., Detroit, Station Complement, Camp Wheeler, Macon, Ga.
GLOSS, Kenneth E., 1st Lieut., Crystal Falls, Mich., Air Corps Basic Flying School, San Angelo, Texas.
HALE, Claude E., 1st Lieut., Marshall, Mich., Station Hospital, Fort Sam Houston, Texas.
HANNAN, Kenneth D. L., 1st Lieut., Prairie Du Sac, Wis., 27th Division, Fort McClellan, Ala.
HANSEN, Harvey C., 1st Lieut., Battle Creek, Mich., 24th Infantry, Fort Benning, Ga.
HARPER, Jesse T., Captain, Detroit, Station Hospital, Fort Custer, Mich.
HORA, James L., 1st Lieut., Chicago, 27th Division, Fort McClellan, Ala.
HOROWITZ, Samuel F., 1st Lieut., Bay City, Mich., Station Complement, Camp Croft, S. C.
HUTCHISON, William A., 1st Lieut., Chicago, Station Complement, Selfridge Field, Mich.
IVKOVICH, Paul, 1st Lieut., Evart, Mich., Station Complement, Camp Croft, S. C.
KANTER, Myron F., 1st Lieut., Chicago, Station Complement, Camp Davis, N. C.
KNAPP, Joseph L., 1st Lieut., Traverse City, Mich., Station Complement, Camp Croft, S. C.
LIVINGSTON, A. Edward, 1st Lieut., Denver, Station Hospital, Fort Sill, Okla.
LOGSDON, Robert E., 1st Lieut., Mount Sterling, Ill., Station Hospital, Fort Sill, Okla.
LONGWELL, Charles W., 1st Lieut., Nashville, Ill., Station Hospital, Fort Bliss, Texas.
LOOMIS, Frederic G., 1st Lieut., Waterloo, Iowa, Station Complement, Camp Shelby, Miss.
MILLER, Harold A., 1st Lieut., Saline, Mich., 23d Evacuation Hosp., Fort Custer, Mich.
MAERCKLEIN, Arthur G., Captain, Union Grove, Wis., Station Complement, Camp Davis, N. C.
MOORE, Gregory P., Captain, Cadillac, Mich., 94th Engineer, Battalion, Fort Custer, Mich.
MUMLER, William C., 1st Lieut., Chicago, Station Hospital, Fort Sheridan, Ill.
MUSSELMAN, Merle M., 1st Lieut., Ann Arbor, Mich., Station Hospital, Fort Bliss, Texas.
NESBITT, William E., 1st Lieut., Alpena, Mich., Station Complement, Camp Wheeler, Ga.
OLTMAN, Diedrich L., 1st Lieut., East Moline, Ill., Station Hospital, Fort Sam Houston, Texas.
OSBORNE, Charles E., 1st Lieut., Vicksburg, Mich., Station Complement, Camp Wheeler, Ga.
PALERMO, Amiel L., 1st Lieut., Chicago, Station Hospital, Fort Bliss, Texas.
PERNWORTH, Paul H., 1st Lieut., Venice, Ill., Scott Field, Ill.
PHILLIPS, Francis J., 1st Lieut., Detroit, Station Complement, Camp Croft, S. C.
POINDEXTER, Marlin H., Jr., 1st Lieut., Milwaukee, Station Complement, Camp Croft, S. C.
PRZYGOCKI, Stanley F., Captain, Chicago, Station Complement, Camp Davis, N. C.
RICHARDS, Francis L., 1st Lieut., Kearney, Neb., Station Complement, Camp Davis, N. C.
RICKETTS, Frederick J., 1st Lieut., Sadorus, Ill., Selfridge Field, Mich.
RODHOLM, Ansgar K., 1st Lieut., Chicago, Station Complement, Camp Croft, S. C.
ROSE, Frederick E., Captain, Millstadt, Ill., Station Complement, Camp Wheeler, Ga.
ROYER, Charles W., 1st Lieut., Battle Creek, Mich., Station Hospital, Fort Sam Houston, Texas.
RUDENS, Maurice C., 1st Lieut., Chicago, Station Hospital, Fort Sill, Okla.
SEIDMAN, Leon H., 1st Lieut., Chicago, Station Complement, Camp Croft, S. C.
SHABART, Elmer J., 1st Lieut., Fort Sheridan, Ill., Station Complement, Camp Wheeler, Ga.
SHAPIRO, Maynard I., 1st Lieut., Chicago, Station Complement, Fort Jackson, S. C.
SHULMAN, Herbert, 1st Lieut., Madison, Wis., Station Complement, Camp Croft, S. C.
SIBRAWS, William A., 1st Lieut., East Detroit, Mich., Station Complement, Fort Jackson, S. C.
SIEGEL, Irving, 1st Lieut., Chicago, Randolph Field, Texas.
SIMENSON, Raymond S., 1st Lieut., Valders, Wis., Medical Replacement Center, Camp Grant, Ill.
TARRE, Harold I., 1st Lieut., Chicago, 24th Infantry, Fort Benning, Ga.
THORNBURG, William M., 1st Lieut., DuQuoin, Ill., Station Hospital, Selfridge Field, Mich.
THORNTON, John C., Jr., 1st Lieut., Brownsville, Tenn., Station Hospital, Fort Sill, Okla.
TIMRECK, Harold A., 1st Lieut., Beaverton, Mich., Station Hospital, Fort Sam Houston, Texas.
WIENER, Israel, 1st Lieut., Detroit, 24th Infantry, Fort Benning, Ga.
WILLIAMSON, Edwin M., 1st Lieut., Detroit, Station Complement, Camp Wheeler, Ga.
WOOD, Cordelle A., Major, Waukesha, Wis., 5th Division, Fort Custer, Mich.
WORDEN, Robert W., 1st Lieut., Chicago, 207th General Hospital, Camp Livingston, La.

AVIATION MEDICINE

The Los Angeles County Medical Association devoted its May 29 meeting to a discussion of aviation medicine. Dr. Isaac H. Jones opened the discussion; other speakers participating in the discussion were Lieut. Col. Ernest F. Harrison, flight surgeon, U. S. Army Air Corps; Comdr. Joel J. White, flight surgeon, U. S. Navy; Lieut. Comdr. John H. Korb, flight surgeon, U. S. Navy, and Dr. Robert W. Langley.

MEDICAL OFFICERS WHO DESIRE TO ATTEND MEETINGS

The War Department has announced that officers of the medical department who desire to attend meetings of any of the national societies pertaining to their profession will be permitted to attend these meetings on detached service status and without expense to the government, provided their services can be spared.

ORGANIZATION SECTION

OFFICIAL NOTES

RADIO PROGRAM AT CLEVELAND

The customary arrangements for radio broadcasts in connection with the annual session of the American Medical Association, at Cleveland, have been made.

The weekly dramatized program Doctors at Work, on the Blue network of the National Broadcasting Company, will close with the broadcast scheduled for Wednesday, June 4 at 10:30 p. m., Eastern daylight saving time, with a program entitled "March of Medicine, 1941." The dramatic episodes and music will originate at Chicago, as usual, but the summary will be delivered from the studios of WHK at Cleveland.

In addition, the following broadcasts have been scheduled on National Broadcasting Company and Columbia Broadcasting System networks, and Cleveland local stations:

WTAM-NBC. Monday, June 2. 7:45 p. m., eastern daylight saving time. Dr. N. B. Van Etten, New York. Medical progress and national defense.

WTAM. Wednesday, June 4. 10-10:15 p. m., eastern standard time. Dr. Lowell S. Selling, Detroit. Psychology of traffic offenses.

WTAM. Tuesday, June 3. 10:15-10:30 p. m., eastern standard time. Dr. John D. Currence, New York. Arthritis.

WTAM-NBC (Blue). Friday, June 6. 10-10:15 p. m., eastern daylight saving time. Dr. W. W. Bauer, Chicago. Convention news.

WHK. Tuesday, June 3. 11:15-11:30 a. m., eastern standard time. Dr. M. S. White, Randolph Field, Texas. Medical aspects of flying.

WHK. Thursday, June 5. 11:15-11:30 a. m., eastern standard time. Dr. J. West Mitchell, Sewickley, Pa. Diabetes.

WGAR-CBS. Wednesday, June 4. 9:15-9:30 p. m., eastern standard time. Dr. Frank H. Lahey, Boston. Progress in medicine and surgery.

WGAR-CBS. Thursday, June 5. Dr. W. W. Bauer. Science Service program. See local papers for time.

WGAR. Tuesday, June 3. 4:15-4:30 p. m., eastern standard time. Dr. Grover C. Penberthy, Detroit. The treatment of burns.

WGAR. Thursday, June 5. 4:15-4:30 p. m., eastern standard time. Dr. Gordon B. New, Rochester, Minn. The treatment of face injuries.

WCLE. Wednesday, June 4. 1:15-1:30 p. m., eastern standard time. Dr. Walter C. Alvarez, Rochester, Minn. Food allergies.

WCLE. Tuesday, June 3. 1:15-1:30 p. m., eastern standard time. Dr. G. Wilse Robinson Jr., Kansas City, Mo. Old age.

WTAM. Tuesday, June 3. 4:45-5 p. m. Woman's Club of the Air. Miss Jane Weaver, Cleveland, and Dr. W. W. Bauer, Chicago.

WTAM. Sunday, June 1. 2:2:15 p. m., eastern standard time. Dr. Morris Fishbein, Chicago. Preview of the convention.

Special broadcasts for the children in Cleveland and suburban schools have been scheduled on the short wave radio station WBOE, operated by the Cleveland Board of Education, as follows:

1. Wednesday, June 4. 2:10-2:25 p. m., eastern standard time. Dr. M. E. Obermayer, Chicago. Skin and adolescence.

2. Thursday, 10:30-10:45 a. m. Dr. Sara M. Jordan, Boston. Constipation and laxatives.

MEDICAL ECONOMIC ABSTRACTS

MEDICAL CARE FOR THE AGED IN WASHINGTON

A REPORT BY THE BUREAU OF MEDICAL ECONOMICS

At the election held in the state of Washington, Nov. 5, 1940 Initiative No. 141 providing for an old age pension of not less than $40 a month including any other income of the recipients was adopted by a vote of 358,009 with 258,819 against it. It is expected that the federal government will contribute one half, or $20, and the measure provides that in case the federal contribution is increased the state shall add a sum equal to whatever the federal subsidy may be. A section of the law which seems to have attracted little attention when the initiative was under discussion says:

> In addition to Senior Citizen Grants, the Department shall provide for those eligible medical, dental, surgical, optical, hospital and nursing care by a doctor of recipient's own choosing; and shall also provide artificial limbs, eyes, hearing aids and other needed appliances.

Although at the time the law was enacted there were only 45,000 persons receiving an old age pension, the Social Security Department has since accepted 15,000 more, making a total of 60,000 old age recipients. It is now thought that the total number of recipients may reach 70,000 or possibly 75,000. The state must bear the entire expense of the medical care furnished. When the budget was first made up in December 1940 an item of $4,320,000 was included. The Washington State Medical Association after studying the provisions of the act concluded that a minimum of $9,700,000 would be required to provide medical care to 45,000 recipients. The governor finally recommended an appropriation of $5,320,000, which in his opinion would be sufficient. Of this amount 50 per cent, or $2,660,000, was definitely earmarked for doctors' services. The attorney general ruled that the word "doctor" would include doctors of medicine, dentists, osteopaths, chiropractors and chiropodists.

The act is to be administered by the State Medical-Dental Board of the State Department of Social Security. Nine members of this board have already been appointed, and an additional one is to be appointed by the State Hospital Association. Of those appointed, two physicians were approved by the Washington State Medical Association, two physicians appointed by the State Department of Social Security, two dentists approved by the State Dental Association, one physician by the State Department of Health, one registered nurse to represent the State Nurses Association and one layman who is assistant to the director of the State Department of Social Security. An interesting feature of the administrative machinery is that the agencies chosen for providing the medical service are the medical service bureaus operated by the county medical societies. There are fourteen of these listed in the regulations. A majority of these provide service in two or more counties, so that almost the entire state of Washington is within the field covered by some medical-dental service bureaus. The plan operates under a fee schedule submitted by the Washington State Medical Association as follows:

First office or home visit	$3.00
Subsequent home visits	2.50
Subsequent office visits	2.00
Night calls from 9 p. m. to 7 a. m.	4.50
Consultation	3.00
Roentgenograms and laboratory work, except in emergencies, shall be authorized by the Medical Service Bureau and shall be at the State Department of Labor and Industries' rates and subject to the same proration as other fees.	
Eye examinations with refraction	5.00

However, this fee schedule is to be paid on the unit system by which the available funds are to be prorated monthly. The medical service bureaus are permitted to make a service charge not to exceed 7 per cent of the bills submitted. There is to be free choice of physicians, osteopaths or chiropractors among all those who agree to abide by the regulations. Hospital care, however, will be provided in county hospitals, and medical care within the hospital will be given by the hospital staff and not by the patient's chosen physician. Prescriptions are not

Information taken from Initiative Measure 141, the mimeographed regulations for the conduct of the act, Northwest Medicine 40:151 (April) 1941, and a letter from Dr. V. W. Spickard, secretary-treasurer of the Washington State Medical Association.

paid for. Medical and optical care will be given. In acute illnesses recipients are limited to seven visits, after which additional authorization must be obtained. In chronic cases care is limited to one visit a week for a period not to exceed three months. Appliances, including glasses, will be provided through the county welfare department within the limits of available funds.

THE BRITISH REGIONAL HOSPITAL SCHEME

In January the Nuffield Provincial Hospital Trust published a proposed scheme for a regional reorganization of British hospitals, which has given rise not only to a great deal of discussion but to some important steps toward its realization.[1] The policy of the trust is briefly described as follows:

(*a*) To divide the country into a number of regions with the object of establishing in each an organization of hospital and health services through a regional council representing the voluntary hospitals and local authorities within the region. It is intended that a hospital or group of hospitals associated with a university medical school should be the regional center whenever possible and the region should be subdivided into two, three or more divisions based on a "key" hospital, each with a divisional hospitals council appointing representatives on the regional council.

(*b*) To give financial aid to the initiation and support of these regional councils.

(*c*) To allot, on application, to such regional or divisional councils sums of money for the promotion of hospital and health services, medical research and teaching which, in the opinion of the regional council, are necessary to meet the needs of the population in the region.

Regional hospital councils have already been constituted in three different parts of the country. The regional councils in these districts have undertaken the following activities:

(*a*) Survey of hospital services on a regional or divisional basis with the object of preparing a comprehensive report on the existence of duplication or over lapping or the necessity for the development of new services or the extension of services already available.

(*b*) Organization of a system of transfer of patients from the "key" hospital to other hospitals within the division after operation or for the continuation of treatment. The result of this arrangement is to reduce the period of occupation of beds in the "key" hospital, thus freeing these beds for other patients requiring such specialist treatment as is unobtainable in other hospitals in the division. It is hoped that this system will reduce waiting lists and thus be of great benefit to the community.

(*c*) Organization of divisional blood transfusion services.

(*d*) Organization of a divisional system of ear, nose and throat clinics. This arrangement is intended to provide a system of clinics in a number of district hospitals in affiliation to the ear, nose and throat department of the "key" hospital in the division.

(*e*) Proposals are under consideration for (1) regional or divisional accident services, (2) regional pathologic services and, in connection with the latter proposals, it is considered that a pathologic service is not only urgently necessary but is peculiarly well adapted to regional organization.

The plan assumes the formation of a primary or key hospital or group of hospitals which should, if possible, be connected with a medical school. The smaller hospitals, generally with less than twenty beds, within each region are to be linked up with the key hospitals with the understanding that the smaller hospital should undertake the care of patients from their neighborhood "who do not need more special skill than can be obtained locally or by visits of specialists from the center and who are ready to leave the key hospital and are not yet fit to return to their homes." It proposed that the key hospitals shall be linked with the smaller institutions by a system of periodic visits by the consulting staff of the key hospitals and the organization of special services, such as pathologic, accident and cancer, on a regional basis.

The growth of municipal hospitals since the local government act of 1929 has proceeded to the point at which they now have more beds than the voluntary hospitals. It is proposed to include both municipal and voluntary hospitals in the plan and to establish regional medical advisory committees representative of the various branches of the medical profession. These advisory committees will have the responsibility of advising the regional councils with regard to the development, the limitation or the curtailment of services in order to avoid wasteful overlapping or competition.

1. Buzzard, Sir E. Farquhar, Chairman of the Medical Advisory Council of the Trust: Post-War Hospital Policy, The Nuffield Provincial Hospital Trust at Work, Lancet **1**:155 (Feb. 1) 1941.

MEDICAL LEGISLATION

STATE MEDICAL LEGISLATION

Connecticut

Bill Introduced.—Substitute for H. 1813 proposes to permit a registered physician to advise and prescribe for married persons regarding marriage problems and to give such persons access to medical information and supplies conducive to health, notwithstanding the restrictions contained in the laws of Connecticut relating to the use of drugs or instruments for the prevention of conception.

Florida

Bill Introduced.—H. 1230, to amend the medical practice act, proposes to eliminate those provisions which require that, of the ten members of the board of medical examiners, five shall be allopathic physicians, three, eclectic physicians and two, homeopathic physicians.

Illinois

Bill Introduced.—H. 809 proposes to enact a new chiropody practice act. The bill proposes that "A person practices chiropody within the meaning of this Act who offers or undertakes, by any means or method, to diagnose, recommend, or prescribe for any ailment or supposed ailment of the human foot of another or who offers or undertakes the local, medical, mechanical or surgical treatment of any ailment or supposed ailment of the human foot of another including general manipulative massage, whether manual, mechanical or electrical, except amputation of the foot or toes or the use of anesthetics other than local, or the use of drugs or medicines other than local anesthetics."

DISTRICT OF COLUMBIA

Bill Introduced.—H. R. 4786, introduced by Representative Randolph, West Virginia, proposes to require examination and laboratory tests for syphilis, gonorrhea and tuberculosis of all applicants for marriage licenses in the District of Columbia.

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. R. 4258 has passed the House, providing that whoever brings on board or has in his possession or control on board any vessel of the United States any narcotic drug not constituting a part of the cargo entered in the manifest or part of the ship stores shall be subject to fine or imprisonment, or both. H. R. 4293 has passed the House, providing that any person who furnishes blood for transfusion into the veins of any person entitled to undergo treatment at government expense or who shall furnish blood for blood banks or for other scientific and research purposes shall be entitled to be paid therefor a sum not to exceed $50 for each blood withdrawal. The Senate Committee on Public Buildings and Grounds has concluded hearings on H. R. 4545, a bill to provide for the acquisition and equipment of public works made necessary by the defense program, including the acquisition and equipment of hospitals. S. 194 has been passed by the Senate, proposing to authorize research by the United States Public Health Service relating to the cause, diagnosis and treatment of dental diseases.

Bills Introduced.—S. 1527, introduced by Senator Smathers, and H. R. 4789, introduced by Representative Wene, both of New Jersey, propose a federal appropriation of $4,000,000 to construct a veterans' hospital in New Jersey with a capacity of not less than one thousand beds. H. R. 4770, introduced, by request, by Representative May, Kentucky, proposes to amend the Selective Training and Service Act so as to authorize the President to provide for the deferment, by age group, from training and service under the act of those men whose ages are such that he finds that deferment to be advisable in the national interest. H. R. 4793, introduced by Representative O'Brien, Michigan, proposes an annual appropriation of $50,000,000 to provide rehabilitation and employment for needy physically handicapped persons.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS EPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS AND ARTICLES APPEAR IN THE STUDENT SECTION, PAGE 2543.

CALIFORNIA

Society News.—The Junior Section of the Los Angeles County Medical Association and the Junior Bar Association of Los Angeles held a joint symposium, May 15.——Dr. Joseph Brennemann, Los Angeles, discussed "Appendicitis in Childhood" before the Hollywood Academy of Medicine, May 8.

Flower Show Society.—The *Bulletin* of the Los Angeles County Medical Association announces that a Physicians' Flower Show Society will be formed, evidencing the success of the society's first flower show, held April 16-17. A section will be created within the new society especially for the wives of members who are interested in flower arrangements. The bulletin also announced a two day exhibit to be held this fall during the chrysanthemum season.

DELAWARE

Appointments at du Pont Institute.—Dr. Daniel Murray Angevine, assistant professor of pathology at Cornell University Medical College, New York, was appointed bacteriologist and pathologist at the Alfred I. du Pont Institute of the Nemours Foundation at Wilmington, effective May 1. According to *Science*, other appointments that have been made recently include Dr. Lee E. Farr, associate in medicine at the Hospital of the Rockefeller Institute for Medical Research, New York, as director of research and pediatrician-in-chief. He became at the same time visiting associate professor of pediatrics at the University of Pennsylvania School of Medicine, Philadelphia. Dr. Douglas A. MacFadyen, associate in chemistry at the Rockefeller Hospital, has been appointed chief of biochemistry at the du Pont Institute and visiting assistant professor of pediatrics at Pennsylvania.

FLORIDA

Personal.—Dr. Leland H. Dame, Jasper, has been named health officer for Highlands and Glades counties, succeeding Dr. Erwin F. Hoffman, Sebring, resigned.——W. C. McLeod, D.D.S., Pensacola, has been appointed a member of the merit system council for the state board of health and the crippled children's commission; the council is to establish general policies for the administration of the merit system under which employees of the board and commission will work.

State Medical Election.—Dr. Gilbert S. Osincup, Orlando, was named president-elect of the Florida Medical Association at its annual meeting recently and Dr. Walter C. Jones Jr., Miami, was installed as president. Other officers of the association include Drs. Luther W. Holloway, Jacksonville, Frederick K. Herpel, West Palm Beach, Walter C. Payne, Pensacola, vice presidents; Dr. Shaler A. Richardson, Jacksonville, secretary-treasurer, and Stewart G. Thompson, D.P.H., Jacksonville, managing director. The 1942 session will be in West Palm Beach.

IDAHO

State Medical Meeting in Sun Valley.—The forty-ninth annual session of the Idaho State Medical Association will be held at the Sun Valley Lodge, Sun Valley, June 18-21, under the presidency of Dr. Abram M. Newton, Pocatello. Guest speakers will include the following members of Stanford University School of Medicine, San Francisco:

Dr. William Dock, Etiology and Pathology of Hypertension; Causes of Peptic Ulcer and Their Control; Cancer from the Pathologist's Angle.
Dr. David A. Rytand, Management of Hypertension; Management of Bright's Disease; Nature and Treatment of Obesity.
Dr. Maurice L. Tainter, Practical Application of Sympathomimetic Drugs Including Benzedrine; New Remedies Used in Gastrointestinal Disease, Including Colloid Laxatives; Medicinal Treatment of Asthma and Other Allergies; Present Status of Sulfonamide Derivatives.
Dr. Carleton Mathewson Jr., Diagnosis and Treatment of Bowel Obstruction; Surgical Treatment of Peptic Ulcer; Ambulatory Treatment of Fractures of the Lower Extremity.
Dr. Nelson J. Howard, The Endocrine Basis of Benign Lesions of the Breast; Pathology and Clinical Features of Disease of Tendons; Common Injuries to the Heart.

In addition, instruction courses will be conducted by members of the state medical association. A round table luncheon is planned for each day. Golf and bowling tournaments are also on this year's program.

ILLINOIS

Survey of Crippled Children.—Information has been collected on more than 32,000 crippled children in the state through a survey now nearing completion by the WPA and the state division for handicapped children. Details cover the crippling condition, race, sex, age and county of residence, providing data on an exceptionally large group of cases for research studies and establishing the basis for a more nearly complete current registry of crippled children throughout the state. The maintenance of a current registry is required by the U. S. Children's Bureau of the state division charged with giving services to crippled children under the provisions of the social security act.

Chicago

Hospital News.—Construction has been started on a new $300,000 addition to the Mount Sinai Hospital to house the new pediatric department, semiprivate facilities for white collar workers and deluxe private room accommodations. A new morgue and necropsy room and a new ambulance entrance with adjoining emergency room will also be built.

Meeting of Academy of Sciences.—Dr. Nathan Smith Davis III was reelected president of the Chicago Academy of Sciences at its eighty-fourth annual meeting, April 14. The speaker of the evening, Dr. Andrew C. Ivy, whose address was entitled "The Gastrointestinal Hormones and Their Uses," was elected an honorary member of the academy.

University News.—Reuben L. Kahn, Sc.D., assistant professor of bacteriology and serology in charge of clinical laboratories, University of Michigan Medical School, Ann Arbor, lectured at Mercy Hospital, April 25, under the auspices of the department of preventive medicine, public health and bacteriology, Loyola University School of Medicine. His subject was "Newer Observations in the Serology of Syphilis."

Personal.—Dr. James H. Hutton has been appointed state health consultant of the National Youth Administration for Illinois; he will direct the procedure for physical examinations of NYA youth in the state.——Dr. Earl E. Kleinschmidt, associate professor and chairman of the department of public health, preventive medicine and bacteriology at Loyola University School of Medicine, has been granted leave of absence for three months to work in Washington making plans for the protection and guidance of students employed in vocational training for defense work in industry.

The Cappa Prize.—The Institute of Medicine of Chicago offers a prize of $400 for the most meritorious investigation in medicine or in the specialties of medicine. The investigation may be also in the fundamental sciences, provided the work has a definite bearing on some medical problem. Competition is open to graduates of Chicago medical schools who completed their internship or one year of laboratory work in 1939 or thereafter. Manuscripts must be submitted to the secretary of the institute, 86 East Randolph Street, not later than December 31. If no paper is deemed worthy of the prize, the award may be withheld at the discretion of the board of governors.

IOWA

Personal.—Dr. Wallace S. Petty, Sioux City, has resigned as health officer of Woodbury County. He has been succeeded by Dr. John A. Cowan, who has been acting director of public health for Sioux City and Woodbury County.——Dr. James E. Dyson has been appointed acting director of health of the public schools of Des Moines. He fills the vacancy that occurred when Dr. Fred Moore died recently. Dr. Dyson graduated at the University of Minnesota Medical School, Minneapolis, in 1916.——Dr. David T. Nicoll, Mitchellville, was recently made a life member of the Polk County Medical Society on his completion of fifty years in the practice of medicine.

Society News.—The Calhoun County Medical Society was addressed in Rockwell City, April 15, by the following physicians from Council Bluffs; Drs. McMicken Hanchett, "Treatment of Tetanus"; Aldis A. Johnson, "Newer Procedures in Diagnostic Medicine," and Jack V. Treynor, "Treatment of Subacute Throat Infections."——Dr. Henry G. Decker, Des Moines, discussed "Relief of Intractable Pain" before the Humboldt County Medical Society in Humboldt, April 17.——Dr. Rolland Russell Best, Omaha, addressed the Johnson County Medical Society, April 2, in Iowa City on "Applica-

tion of the Biliary Flush in the Treatment of Biliary Tract Disease." —— Dr. Irvine McQuarrie, Minneapolis, discussed "Experiments of Nature in Clinical Medicine" before the Linn County Medical Society, April 10, in Cedar Rapids.

MAINE

Society News.—A symposium on lesions of the stomach and duodenum was presented before the Portland Medical Club, April 1, by Drs. Elton R. Blaisdell and Jack Spencer; papers were presented by Drs. George A. Tibbetts and Isaac M. Webber on "Acute Surgical Emergencies" and "Gastric Resection" respectively. —— Dr. Donald Munro, Boston, discussed "Immediate Treatment of Head Injuries" before the Kennebec County Medical Association in Augusta, April 17. —— The Knox County Medical Association was addressed in Rockland, April 8, by Dr. Katherine S. Andrews, Boston, on "Gastric Cancer."——The York County Medical Association devoted its meeting in Sanford, April 2, to a panel discussion on endocrine dysfunction. Participating were Drs. James Carswell Jr. and Howard L. Apollonio, Camden, and Paul A. Jones, Union.

MASSACHUSETTS

The Henry Jackson Lecture.—Comdr. John R. Poppen, bureau of aeronautics, U. S. Navy Department, Washington, D. C., delivered the Henry Jackson Lecture for 1941, under the auspices of the New England Heart Association, May 2. His subject was "Cardiovascular Problems in Aviation Medicine."

Fellowship Awarded. — Dr. Israel Kapnick, Providence, R. I., now studying at the Massachusetts General Hospital, Boston, has been awarded the Louis E. Kirstein Fellowship at Harvard Medical School for the summer of 1941. The Kirstein Fellowship, to promote "scientific medical education," was established through a gift of $28,550 made to Harvard University by eighty-nine friends of Mr. Kirstein, vice president of William Filene's Sons Company, in honor of his seventieth birthday and in recognition "of their affection for him as a man and their admiration of him as a humanitarian." In accordance with the request of the donors, the fund remains active so that additions may be made to it from time to time. Dr. Kapnick graduated at Harvard in 1938.

MINNESOTA

The Root Medical History Lecture.—Dr. Arno B. Luckhardt, professor of physiology, Department of Medicine, University of Chicago, delivered the annual William W. Root Medical History Lecture at the University of Minnesota Medical School, Minneapolis, April 29. The lecture is sponsored by Alpha Omega Alpha Fraternity. His subject was "Dr. William Beaumont and the Medical Epic of Northwest Territory."

University News.—A course in roentgen diagnosis of nontuberculous diseases of the lungs and pleura was offered at the Center for Continuation Study, University of Minnesota, Minneapolis, May 22-24. Enrolment was limited to physicians with special training in radiology.——The Carnegie Corporation has made a grant of $5,000 to the University of Minnesota for the continued support of investigations of viruses in relation to cell growth, conducted under the direction of Dr. Robert G. Green, professor of bacteriology and immunology at the medical school.

Society News. — Carl G. Hartman, Ph.D., Baltimore, addressed the Hennepin County Medical Society, Minneapolis, April 7, on the "Use of Gonadotropic Substances in Gynecology (based largely on controlled experiments in the monkey) and Administration of Steroidal Hormones in the Form of Pellets (Estrogen Therapy) and Possible Carcinogenesis."—— The Minnesota Pathological Society was addressed in Minneapolis, April 12, by Drs. Robert G. Green and Charles A. Evans on "Vitamin B Deficiency from Fish Diets" and Elexious T. Bell, "Pathologic Physiology of the Kidney." All are of Minneapolis. —— Dr. Max W. Alberts, St. Paul, discussed "Complicating Factors Associated with Cancer of the Large Bowel" before the Minnesota Academy of Medicine in St. Paul, April 9.

NEBRASKA

Lecture by Dr. Dam.—Professor Henrik Dam of the Biochemical Institute, Copenhagen, Denmark, addressed a special meeting of the Lancaster County Medical Society, Lincoln, April 10, on "Clinical Aspects of Vitamin K."

Personal.—Dr. George E. Charlton, superintendent of the Norfolk State Hospital, Norfolk, was recently honored by a reception marking his twenty-fifth year of association with the hospital. He was appointed superintendent in 1916 and has served continuously since that time except for two years when he was superintendent at the Hastings State Hospital at Ingleside.

NEW YORK

Society News.—Dr. Sumner L. S. Koch, Chicago, was the guest speaker at a meeting of the Western New York Surgical Association at Jamestown, April 10, on "Injuries of the Hand." An afternoon session was devoted to round table discussions. ——Dr. Cary Eggleston, New York, addressed the Medical Society of the County of Albany, April 23, on "Current Concepts of Coronary Artery Disease and Myocardial Infarction." ——Dr. Howard T. Karsner, Cleveland, addressed the Onondaga County Medical Society in a joint meeting with Alpha Omega Alpha, Syracuse, April 1, on "Calcific Sclerosis of the Aortic Valve."——Dr. Varaztad H. Kazanjian, Boston, addressed a joint meeting of the Syracuse Academy of Medicine and the Eye, Ear, Nose and Throat Club, April 15, on "Traumatic Surgery of the Face and Jaws, Including War Injuries."

New York City

Personal.—Dr. James L. McCartney, formerly with Sharp & Dohme, Philadelphia pharmaceutic manufacturers, has been appointed medical director of William R. Warner & Co., Inc., and associated organizations.——Dr. Paul W. Lapidus has been appointed adjunct professor of orthopedic surgery and assistant attending orthopedic surgeon in the New York Polyclinic Medical School and Hospital.

Squibb Award Goes to Anatomist.—Philip E. Smith, Ph.D., professor of anatomy at Columbia University College of Physicians and Surgeons, was presented with the annual Squibb Award during the session of the Association for the Study of Internal Secretions in Atlantic City, May 2-3. The award is given annually by E. R. Squibb and Sons to a "distinguished contributor to the field of endocrinology." Dr. Smith received his degree at Cornell University in 1910. He subsequently served on the faculties of Cornell, California and Stanford universities, becoming professor at Columbia in 1927.

OHIO

Alumni Reunion. — The annual reunion of the Alumni Association of the University of Cincinnati College of Medicine will be held in Cincinnati, June 7. Hospital and clinic demonstrations will be presented during the day and the annual banquet will be held in the evening at the Sinton Hotel. The banquet speaker will be Dr. Clay Ray Murray, associate professor of surgery, Columbia University College of Physicians and Surgeons, New York. Following the banquet there will be a reception and dance in honor of the graduating class. Reservations should be made at the alumni office at the university or at the college of medicine. Dr. Mabel E. Gardner, Middletown, is president of the alumni association.

Dr. Upham Retires as Dean.—Dr. John H. J. Upham, dean of Ohio State University College of Medicine, Columbus, is to be the guest of honor at a testimonial dinner given June 6 at the Neil House by the faculty on the occasion of his retirement. Dr. Upham is retiring because of the automatic age rule of the university. He first joined the faculty in 1897; in 1908 he became professor of medicine and served in that department until he was appointed dean in 1927. Dr. Upham has held many state and national medical offices. In Ohio he was president of the Columbus Academy of Medicine in 1919, president of the Ohio State Medical Association in 1914 and editor of the *Ohio State Medical Journal* from 1907 to 1913. Since 1913 he has been a member of the state board of medical examiners and since 1930 a member of the National Board of Medical Examiners. Dr. Upham was elected to the Judicial Council of the American Medical Association in 1922, then to the Board of Trustees in 1923, serving until 1935, the last two years of that period as chairman of the Board. He was President of the Association for the year 1937-1938.

PENNSYLVANIA

District Meeting.—A meeting of the Seventh Councilor District of the Medical Society of the State of Pennsylvania was held in Williamsport, May 9, with Drs. David E. Hemington, Uniontown, and Walter C. Alvarez, Rochester, Minn., as speakers at the morning session on "Better Medical Care for Workers in Small Industries" and "Puzzling Types of Abdominal Pain" respectively. In the afternoon Dr. Alvarez addressed a joint meeting with the woman's auxiliary of the district on "Why Women Get Nervous." Fifty year awards were made by the president of the state society, Dr. Francis

F. Borzell, Philadelphia, to Drs. Oliver W. H. Glover, Laurelton, Robert B. Tule, Milton, and Lewis E. Wolfe, New Berlin. Dr. Borzell and Dr. Lewis T. Buckman, Wilkes-Barre, president-elect of the state society, discussed subjects of current interest.

Philadelphia

Personal.—Dr. Donald C. Smelzer, director of the Graduate Hospital of the University of Pennsylvania since 1930, will resign, June 1, to become managing director of the Germantown Dispensary and Hospital, according to *Modern Hospital*.

Riesman Memorial Lecture.—The Women's Medical Society of the University of Pennsylvania sponsored the Riesman Memorial Lecture at the University Hospital, May 1. The lecturer was Dr. Sara Murray Jordan, Boston, on "Problems in Modern Gastroenterology."

Haden Society Exhibit.—The Seymour Haden Society recently held its tenth annual exhibition at the University of Pennsylvania School of Medicine. Among the exhibitors were Drs. Isolde T. Zeckwer, Morton McCutcheon, Dale R. Coman and William G. Turnbull. The society was founded by Dr. Edward B. Krumbhaar, professor of pathology. At first the exhibitors were six members of the department of pathology; now members of other departments in the medical school and Philadelphia physicians not connected with the university participate. Originally etchings predominated in the exhibits, but this year oils and sculpture were most numerous.

Lectures on Genetics.—A volunteer lecture course on "Applied Medicogenetics" has recently been presented at the Woman's Medical College of Pennsylvania on Fridays. Clyde E. Keeler, Sc.D., fellow of the Wistar Institute of Anatomy and Biology, University of Pennsylvania, gave the first four addresses and later speakers were:

Charles B. Davenport, Ph.D., Cold Spring Harbor, N. Y., Development of the Eugenic Movement.
Dr. Elizabeth Kirk Rose, Philadelphia, Problems of Marriage and the Family as Met by the Physician.
Dr. Madge T. Macklin, London, Ont., Case Histories from the Medicogenetic Consultation Room.
Frederick Osborn, New York, A Permanent Eugenic Program for the United States.

TEXAS

Personal.—Dr. Sidney B. Hardy, who has been acting administrator of the Jefferson Davis Hospital, Houston, since the resignation of Dr. James H. Stephenson last year, has been appointed superintendent.——Dr. Charles H. McCollum Jr., Fort Worth, recently received the annual distinguished service award of the Fort Worth Junior Chamber of Commerce.

Chemist Honored for Vitamin Research.—Roger J. Williams, Ph.D., professor of chemistry at the University of Texas, Austin, received the $1,000 Mead Johnson and Company prize awarded at the annual meeting of the American Institute of Nutrition in Chicago in April. Dr. Williams was honored "for his outstanding work on the isolation and identification of pantothenic acid." The prize is given for work on the vitamin B complex. Dr. Williams took his doctorate at the University of Chicago in 1919 and has taught chemistry at the University of Oregon and Oregon State College.

Society News.—Drs. Robert R. Shaw and Stuart A. Wallace, among others, addressed the Dallas County Medical Society, Dallas, April 24, on "Pulmonary Lobectomy and Pneumonectomy for Suppurative and Malignant Disease of the Lungs" and "Early Degenerative Lesions of the Pancreas" respectively. Drs. Charles L. Martin and Harry M. Spence, Dallas, were among the speakers, April 10, on "New Radiation Technic for Treatment of Metastatic Cervical Lymph Nodes" and "Surgical Treatment of Ureteral Stones" respectively.——Dr. Titus H. Harris, Galveston, addressed the Jefferson County Medical Society, Beaumont, April 14, on management of the nervous patient.

VIRGINIA

Personal.—Dr. Lee Scott Barksdale has resigned as health officer of Hopewell to enter private practice.——Dr. Guy C. Richardson, Bristol, recently received the distinguished service medal awarded annually by the Bristol Junior Chamber of Commerce to a citizen who has rendered noteworthy community service.——Dr. Julian T. Miller has resigned as health officer of Portsmouth.

Medical College News.—A bronze tablet commemorating the service of Base Hospital No. 45, known as the McGuire Unit, in France during World War I was recently presented to the Medical College of Virginia by the Base Hospital No. 45 Veterans' Association. Dr. William Lowndes Peple, Richmond, made the presentation on behalf of Dr. Stuart McGuire, Richmond, commander of the unit, who was ill, to William T. Sanger, L.H.D., president of the college. The tablet was unveiled by Lockhart Bemiss McGuire, a great-nephew of Dr. McGuire.

State Health Officials Promoted.—Dr. Adrian L. Carson Jr., acting head of the bureau of maternal and child health in the state department of health since the retirement of Dr. Bathurst B. Bagby in July 1940, has been made full director of that bureau, it is reported. Previously he was a member of the staff. Dr. Jack B. Porterfield, who has been state epidemiologist, has been appointed director of the bureau of industrial hygiene. He succeeds Dr. William D. Tillson, now of Parkersburg, W. Va., who resigned several months ago. Dr. Harry H. Henderson, Wheeling, W. Va., has been appointed state epidemiologist to succeed Dr. Porterfield.

GENERAL

Medical Books in the Census of Manufactures.—Books on medicine published in 1939 amounted to 1,868,892 volumes, according to the biennial census of manufactures conducted by the U. S. Bureau of the Census. The annual average since 1925 has been 1,725,000 volumes. The biggest year was 1937, when 3,923,532 volumes were published. The total number of all books published in 1939 was 180,142,492.

Meeting of Radiologists.—The American College of Radiology will hold its annual meeting at the Hotel Statler, Cleveland, June 4. Dr. Henry J. Walton, Baltimore, will deliver his presidential address at the banquet, following the business session. A feature of the banquet this year will be the presentation of the medal for distinguished contributions to radiology to Dr. William Edward Chamberlain, Philadelphia.

Meeting of Postgraduate Committees.—The fifth annual meeting of the Associated State Postgraduate Committees will be held, June 4, at the Hotel Statler, Cleveland. Discussion will be centered on the relation of postgraduate committees to intern instruction in nonteaching hospitals and the possible cooperation in such instruction by members of other organizations. A report on the question of national registry of postgraduate assemblies and a registry for postgraduate instructors will also be presented.

Eradication of Brucellosis.—Forty-five additional counties in thirteen states were declared practically free from brucellosis of cattle, April 1, by the U. S. Department of Agriculture. Counties now in the modified accredited status number three hundred and ninety-one in twenty-three states, the department announced. In the forty-five new counties approximately 533,000 cattle were tested. The greatest number, about 69,500, were in Polk County, Minn.

American Orthopaedic Association.—The annual meeting of the American Orthopaedic Association will be at the Hart House, University of Toronto, June 9-12, under the presidency of Dr. David E. Robertson, Toronto. Included among the speakers will be:

Dr. Frederick R. Wilkinson, Toronto, Osteomyelitis, Recent Experience with Bacteriostatic Drugs.
Dr. Stuart A. Thomson, Toronto, Treatment of Club Feet by the Use of Dennis Brown Splints.
Dr. Joseph S. Barr, Boston, End Result Study of the Treatment of Idiopathic Scoliosis.
Dr. LeRoy C. Abbott, San Francisco, Valgus Deformity of the Knee Resulting from Injury to the Lower Femoral Epiphysis.
Dr. Halford Hallock, New York, Surgical Stabilization of Paralytic Dislocated Hips.
Dr. Robert W. Johnson Jr., Baltimore, Treatment of Acute Osteomyelitis by the Sulfathiazole Drugs.
Drs. Lloyd T. Brown and John G. Kuhns, Boston, Extension Deformities of the Cervical Spine.
Dr. Dallas B. Phemister, Chicago, Resection and Transplantation in the Treatment of Bone Sarcomas.

Painting on Yellow Fever Subject to Be Unveiled.—A painting by Dean Cornwell, the third in the series "Pioneers of American Medicine," will be unveiled during special ceremonies in the Hotel Statler, Cleveland, June 2. The painting shows Major Walter Reed and Dr. Carlos Finlay with Major General Leonard Wood, Dr. Jesse W. Lazear, Dr. James Carroll and Dr. Aristides Agramonte, and John R. Kissinger, first volunteer soldier to be inoculated in the second set of yellow fever experiments. Miss Blossom Reed, daughter of Major Walter Reed, will unveil the painting. Mr. Cornwell chose the yellow fever subject at this time because of its significance in connection with national defense, since the Panama Canal would have been impossible without the success of Finlay and Reed. The series of paintings, depicting outstanding personalities and events in the history of American medicine, will take between ten and fifteen years to complete, one painting

being done a year. Finished paintings are lent to medical schools and medical societies. The first two were "Beaumont and St. Martin" and "Osler at Old Blockley."

Ear, Nose and Throat Meeting.—The American Laryngological, Rhinological and Otological Society will hold its forty-seventh annual meeting at the Ambassador Hotel, Los Angeles, June 16-18, under the presidency of Dr. John MacKenzie Brown, Los Angeles. Speakers will include:

Drs. Fred Z. Havens and Edith M. Parkhill, Rochester, Minn., Malignant Tumors of the Larynx Other Than Squamous Cell Epitheliomas.
Dr. Arthur C. Jones, Boise, Idaho, Report of Carcinoma in the Larynx in a Girl Aged Thirteen.
Dr. Bert E. Hempstead, Rochester, Minn., Treatment and Prognosis of Aural Infections Complicated by Severe Diabetes.
Dr. James Milton Robb, Detroit, A Consideration of the Endocrine Basis for Otosclerosis (candidate's thesis).
Dr. Robert C. Martin, San Francisco, Result of Extirpation of the Sphenopalatine Ganglion.
Dr. Herbert Graebner, New York, Chemotherapy in Acute Nondiphtheritic Laryngotracheobronchitis.
Dr. Emil F. Tholen, Los Angeles, Salivary Calculi.
Dr. Kenneth M. Day, Pittsburgh, Primary Pseudocholesteatomas of the Ear.
Dr. Gabriel Tucker, Philadelphia, Observations on the Interrelationship, Diagnosis and Treatment of Benign and Malignant Tumors of the Larynx, with Special Reference to the Prevention and Cure of Laryngeal Cancer.

Directory of Medical Specialists.—A second edition of the Directory of Medical Specialists has been authorized by the Advisory Board for Medical Specialties, to be ready for distribution in February 1942, with its contents complete to January 1. This directory is the official publication of the board and will list the names of approximately 18,000 diplomates of the fifteen American boards examining candidates for certification in the specialties. This is an increase of 4,000 over the first edition issued early in 1940. The geographic grouping will give completely revised biographic data about each diplomate; there is an alphabetical index with addresses and specialty designations, and the plan of organization, officers and examination requirements of each American board are fully outlined. Information not found in the old edition will be included in the new directory, such as details of formal training and military appointments. The only requisite to inclusion in the directory is formal certification by one of the examining boards. The publication is issued through the Columbia University Press of New York. The secretary of each specialty board serves on the Advisory Editorial Board and Dr. Paul Titus, 1015 Highland Building, Pittsburgh, of the American Board of Obstetrics and Gynecology is the directing editor.

Association for Study of Allergy.—The nineteenth annual meeting of the American Association for the Study of Allergy will be held at the Hotel Cleveland, Cleveland, June 2-3, under the presidency of Dr. Robert L. Benson, Portland, Ore., who will deliver his address Monday on "The Place of Allergy in Internal Medicine." The speakers will include:

Drs. Samuel J. Levin, and Bertha Lillian Shulsky, Detroit, Serological Changes after Oral Ragweed Pollen Therapy in Children.
Oren C. Durham, North Chicago, Ill., A Critical Interpretation of Data on the Incidence of Air-Borne Allergens.
Drs. John M. Sheldon, John Harvey Johnston and Homer A. Howes and Norbert Fell, Ph.D., Ann Arbor, Mich., A Clinical Study of Histamine-Azo-Protein in Allergic Disease.
Dr. Townsend B. Friedman, Dr. John A. Bigler and Marie A. Werner, Chicago, The Immunologic Response of Allergic Children to Toxoid.
Dr. George F. Harsh and Paul B. Donovan, Ph.D., San Diego, Calif., Effect of Wide Variations in K and Na Intake in Asthmatic Patients.

A round table discussion will be held Tuesday afternoon on the use and misuse of drugs. In this group Drs. George Piness, Los Angeles, and Warren T. Vaughan, Richmond, Va., discussing self-administered medication, will present, respectively, "Inhalation of Adrenalin and Benzedrine" and "Ephedrine and Synthetic Derivatives." Dr. Philip D. McMaster of the Rockefeller Institute for Medical Research, New York, has chosen for his subject as the banquet speaker "The Lymphatic Participation in Human Cutaneous Phenomena."

Health Contest Winners Announced.—Winning cities in the twelfth annual health contest conducted by the U. S. Chamber of Commerce in cooperation with the American Public Health Association and with the financial support of the Metropolitan Life Insurance Company were as follows: Baltimore; Evanston, Ill.; Greenwich, Conn.; Hackensack, N. J.; Hartford, Conn.; Honolulu, Hawaii; Madison, Wis.; Memphis, Tenn.; Newton, Mass., and Pasadena, Calif. Winners in the seventh annual rural health contest were the following, chosen from three hundred and thirteen rural health units enrolled: Alcona-Ogemaw-Iosco-Oscoda counties and Alger-Schoolcraft counties in Michigan; Arlington County, Va.; Davidson County, Tenn.; Fayette County, Ky.; Forsyth County, N. C.; Coahoma County, Pike County and Lauderdale County, Miss.; Pickens County, Ala.; El Paso County and Tyler-Smith counties, Texas; Thurston County, Wash., and Wasco County, Ore. The rural health contests are financed by the W. K. Kellogg Foundation of Battle Creek, Mich. In addition, special contests were held for noteworthy achievement in tuberculosis and syphilis control programs. Hartford, Conn., and Newton, Mass., won the contest for the most effective tuberculosis control programs, and the winners for the most effective syphilis control programs were Louisville, Ky.; Chicago; Memphis, Tenn., and Pasadena, Calif.

American Radium Society.—The twenty-sixth annual meeting of the American Radium Society will be held at the Hotel Cleveland, Cleveland, June 2-3, under the presidency of Dr. Frederick W. O'Brien, Boston. Speakers will include:

Drs. John V. Blady and William Edward Chamberlain, Philadelphia, Five Year End Results in Intrinsic and Extrinsic Laryngeal Cancer.
Drs. John E. Leach, Joseph H. Farrow, Frank W. Foote Jr., and Nestor William Wawro, New York, Fibrosis of the Lung Following X-Radiation for Breast Cancer.
Dr. Shields Warren, Boston, Pathologic Aspects of Radiosensitivity of Malignant Tumors.
L. D. Marinelli, M.A., New York, Dosage Determinations with Radioactive Isotopes.
Helen Q. Woodard, Ph.D., and Dr. John M. Kenney, New York, Relation of Phosphatase Activity in Bone Tumors to the Deposition of Radioactive Phosphorus.
Drs. Norman L. Higinbotham and Bradley L. Coley, New York, Effects of Preoperative Irradiation in the Treatment of Patients with Bone Sarcoma.
Dr. Leroy Sante, St. Louis, Pneumoperitoneum as an Aid in Pelvic Irradiation.

The society will award the Janeway Medal to Dr. Edward H. Skinner, Kansas City, Mo., at the annual dinner Monday evening. Dr. Skinner will present the Janeway Lecture on "The Philosophy and Economics of Cancer." The Janeway lecturers are selected because of their outstanding scientific contributions.

Meeting of Broncho-Esophagological Association.—The twenty-fourth annual meeting of the American Broncho-Esophagological Association will be held at the Mid-Day Club, Cleveland, June 3, under the presidency of Dr. Gabriel Tucker, Philadelphia. Subjects to be discussed include:

Dr. Carlos E. Pitkin, Cleveland, Repeated Severe Hemoptysis Necessitating Pulmonectomy.
Dr. Albert H. Andrews Jr., Chicago, Functional Examination of Respiration in Obstructive Diseases.
Dr. Arthur E. Hammond, Detroit, An Intratracheal Tumor Causing Severe Attacks of Dyspnea.
Dr. Maurice Bonnier, Montreal, Canada, Some Interesting Endoscopic Foreign Body Cases.
Dr. Burt R. Shurly, Detroit, A Foreign Body Retained Thirteen Years in the Bronchus.
Dr. George W. Grier, Pittsburgh, Mediastinal Enlargement in Acute Laryngotracheobronchitis.
Dr. Julian Johnson, Philadelphia, Surgical Treatment of Carcinoma of the Esophagus.
Dr. Herman J. Moersch, Rochester, Minn., Further Observations on the Treatment of Esophageal Varices by Injection of a Sclerosing Solution.
Drs. Hugh G. Beatty and Dwight M. Palmer, Columbus, Ohio, Esophageal Neuroses.
Dr. Edward B. Benedict, Boston, Carcinoma of the Esophagus with Special Reference to Treatment by Radical Surgery, X-Ray and Bougienage.
Drs. Chevalier L. Jackson and Frank W. Konzelmann, Philadelphia, So-Called Adenoma of the Bronchus.
Drs. Paul H. Holinger, Chicago, and Ralph G. Rigby, Council, Idaho, Bronchogenic Carcinoma Without Bronchial Obstruction.

Special Society Elections.—Dr. Jesse L. Bollman, Rochester, Minn., was elected president of the American Society for Experimental Pathology at its annual meeting in April; Dr. Baldwin H. E. W. Lucke, Philadelphia, vice president, and Dr. Harry P. Smith, Iowa City, secretary, reelected.—— Dr. Roscoe R. Graham, Toronto, was recently named president-elect of the Central Surgical Association at its inaugural meeting at the University of Michigan, Ann Arbor. Dr. Grover C. Penberthy, Detroit, was installed as president. Other officers include Drs. George M. Curtis, Columbus, Ohio, secretary; Henry K. Ransom, Ann Arbor, recorder; Max M. Zinninger, Cincinnati, treasurer. The second meeting of the association will be held in Chicago, Feb. 27-28, 1942. The Central Surgical Association is designed particularly for a closer relationship of younger surgeons of the midwest and nearby Canadian provinces. Its principal founder was Dr. Roy D. McClure, Detroit, who was the first president of the group. The association was incorporated under the laws of Ohio, January 15. Its membership now totals one hundred and fifty members, including forty-seven founders, distributed over eleven states and three Canadian provinces. —— Dr. Samuel R. Haythorn, Pittsburgh, was elected president of the American Association of Pathologists and Bacteriologists at its annual meeting in New York, April 10. Other officers are Drs. Paul R. Cannon, Chicago, vice president; Howard T. Karsner, Cleveland, secretary, and Alan R. Moritz, Boston, treasurer. The next annual session will be held in St. Louis, April 2-3, 1942.

Foreign Letters

PARIS

(From Our Regular Correspondent)

April 6, 1941.

Invisible Dermatoses

In a recent paper before the Society of Dermatology, Gougerot justified the paradoxic use of the term "invisible dermatosis." He had in mind not so much cutaneous diseases which were invisible as those which exist in unperceived and attenuated form and are likely to become reactivated under changed conditions. This makes their early detection important. Wood's glass, infra-red photography, local leukodermia, pigmentation, ultraviolet irradiation, biopsy and local injections are among the diagnostic measures available. Invisible dermatoses are often associated with visible lesions. Their true nature is often disclosed under treatment and, like the original lesions, they yield to specific therapies. Pruritus, often observed in lichen planus as an isolated sign, can be cured by arsenic given internally and chrysophanic acid given externally. In eczema the harmful antigen induces an allergic pruritus. Some forms of dyshidrosis, urticaria and psoriasis reveal themselves in Wood's glass or by the use of eosin. Here the erythema of measles, scarlatina or syphilis is disclosed before it is seen with the eye. In leprids the injection of methylene blue stains the visible leprid at the same time that it discloses the presence of invisible maculae and is hence an excellent means for early diagnosis. Invisible pathologic phases have both a theoretical and a practical interest and open up questions of pathogenesis, early diagnosis, prognosis, therapy and prophylaxis, for example in eruptive fevers, and constitute one of the best tests of cure.

Procaine Hydrochloride in Disorders Involving the Cervical Sympathetic

According to Dos Ghallos, speaking before the Faculty of Medicine of Paris, the bronchopulmonary innervation is composed of a mass of terminal plexuses in the center of which are found the fibers of the vagus and two of the sympathetic. The lung is therefore a neurovascular organ. This is the reason why a therapeutic attack on the sympathetic seems indicated in many functional disorders of the lungs. In asthma, in the spasmodic cough of tuberculous persons, in bronchorrhea and in the bronchopneumonia of nurslings remedial action by way of the sympathetic may be obtained through the use of procaine hydrochloride. In pulmonary embolism this drug may save life. In asthma, dyspnea and stubborn cough it may have to be used for a longer time and may serve for functional exploration. The effect aimed at is neither sympathicolytic nor vagolytic; it seems rather directed against the peripheral neurohormonal system and to involve, for the most part, a modification of secretory processes.

The author employed procaine hydrochloride in about 200 cases of adults and nurslings and encountered only five failures. Successful injections provoke the Claude Bernard-Horner syndrome and hyperemia in the corresponding superior member as well as in the superior portion of the neighboring thorax. If inadvertently the brachial plexus or the pleural dome has been injured by the needle, a painful cough results, which merely requires the injection to be postponed to the next day. The same is true if a blood vessel is injured; in this case blood will show in the syringe. Some other accidents may also follow drug intoxication. Dos Ghallos does not agree with other investigators who, like White, believe that a combination of alcohol with procaine hydrochloride gives more enduring results. On the contrary, he considers the combination unreliable, dangerous and needlessly painful. His technic is based on that of Leriche. While recognizing the value of procedures which allow reaching the stellate ganglion and the thoracic chain in its upper portion, Dos Ghallos prefers the upper external route of Arnulf, which permits simultaneous infiltration of the stellate ganglion and of the first three or four thoracic ganglions. Procaine hydrochloride is best injected bilaterally in one or two sessions. It is repeated more or less often in accordance with clinical indications, generally two or three times a week. The only contraindications are cardiac insufficiency, which complicates respiratory disorders, pulmonary suppuration and acute pulmonary edema.

BRAZIL

(From Our Regular Correspondent)

March 31, 1941.

A New Antihemorrhagic Agent

Interesting work on snake venom has been done in São Paulo at the famous Butantan Institute. Among the properties of ophidian venom is the coagulating one described by Fontana in 1781. An application of this property for clinical purposes is being used according to the methods of Klobusitsky and König, who obtained the dissociation of the coagulating principles from the toxic ones of the venom. On this basis Eduardo Vaz and Anibal Pereira did experimental work at the Pinheiros Institute, employing a ferment extracted from the venom of species of the Bothrops type. It was demonstrated that the botropase is a therapeutic agent of great activity. Its coagulating effects are obtained by the use of small doses, of which the safe results are as satisfactory in rapidity as in duration. Several clinicians and surgeons confirmed the highly efficient action of the product. In view of this, botropase is widely used in Brazilian hospitals in all cases of hemorrhage. For an immediate effect, botropase can be injected intravenously in doses of 1 cc.; if there is danger of repetition of bleeding, 1 cc. should be injected subcutaneously at once. For prophylaxis a subcutaneous or intramuscular injection of 1 cc. should be given two to three hours before the surgical intervention.

Eduardo Vaz and Anibal Pereira read an article before the São Lucas Medical Society at São Paulo showing that the botropase is the best antihemorrhagic agent. Comparative experiments with other hemocoagulants proved that snake venom is superior, even when diluted 1:100 and used in a five times smaller volume than the others, which means five hundred times less.

The following conclusions were proposed:

1. By means of heating it is possible to separate the toxic from the hemocoagulant dose of the venom of Bothrops jararaca, thus allowing the use, devoid of danger, of a venom solution in the therapeutics of hemorrhages.

2. The heated solution, called botropase, does not alter the white corpuscles or the red ones, it shows no proteolytic properties in vitro and in vivo, and it does not cause local lesions or intoxications.

3. The hemocoagulating activity is extraordinary, 0.0002 cc. for the pigeon representing 0.0002 mg. of venom, which is a six thousand times smaller dose than the toxic one for this animal.

4. Botropase does not exhibit the negative phase which can be observed with other venom solutions.

Personal

The medical centers of São Paulo commemorated lately the professoral jubilee of Antonio Almeida Prado. All the medical societies held a solemn meeting, with the cooperation of the Faculty of Medicine and other official institutions. Professor Almeida Prado is well known by his works on mixed cerebellar syndromes and the publication of several medical books.

NEWS FROM GERMANY

(Compiled from recent German periodicals)

Matriculation of German Students

According to a decree, students of German origin within the conquered and annexed western provinces (Alsace, Lorraine and Luxembourg) are required to matriculate at certain designated universities. The explanation is that the difference in school systems under which the now repatriated students were taught does not fit in with the German pattern and requires the organization of introductory courses to prepare them for the German system. These introductory courses cannot be offered promiscuously. Hence Alsatian German students will matriculate in Frankfort, Freiburg, Marburg and Tübingen; those from Lorraine in Heidelberg, Marburg and Leipzig, and those from Luxembourg in Bonn, Cologne, Giessen, Munich and Innsbruck. The decree will be effective until the beginning of the winter semester 1941-1942.

Medical Education in Alsace as Seen Through German Eyes

In the *Deutsche medizinische Wochenschrift*, Babillotte compares the medical training at the university of Strasbourg, conducted according to the French university system, with that of the vaunted German system. The Alsatian university pattern is considered as conforming in organization and spirit to the secondary school system, in which attendance and progress are constantly checked and intellectual independence is inhibited. The French-Alsatian system was characterized by numerous tests and competitive examinations. This made it difficult for students to transfer to other universities, as is customary in Germany. The writer concedes that the French-Alsation system kept the students "on their toes" and tended to prevent the development of academic hoboes such as used to be plentiful on German university campuses.

In the university of Strasbourg the medical curriculum was fully planned and had to be followed. Electives did not exist. A premedical year was devoted to physics, chemistry, botany and zoology. Clinical studies were begun in the second year. The student might also apply for assignment as assistant during the second year. During the third year the student had to be assigned as an assistant in surgery or internal medicine. Obligatory assistantship continued also through the fourth year. Final examinations were given on all subjects. Pharmacology, medical jurisprudence, psychiatry, therapeutics, hydrology and hygiene were reserved for the fifth year. The assistant served his time during this year in the ear and eye or the children's clinics. Final examinations were divided into three parts. The doctoral dissertation was generally prepared several years after the completion of the finals. The dissertation constituted the official medical diploma. Its recording by the health department signified admission to medical practice.

Great importance was attached to these assistantships, only twenty of which were available annually. These were awarded after competitive examinations based on histology, physiology and clinical subjects. Those selected were called externs and assisted in the wards, laboratories and at operations. After spending two years as an extern the student was admitted to competitive examinations, which qualified him for the internship (equivalent to the position of assistant physician in the German system). The salary was 500 francs (25 reichsmarks) with free board and lodging. The internship lasted four years. At the end of the four years one was eligible, if there was a vacancy, for the position as head of a clinic, which was good for two years. Vacancies were filled by appointment by the director of the clinic.

The author points out other deficiencies inherent in French universities, such as the statement that no provision was made for sports, good fellowship or social and political activities. His comment, however, is focused on the "ridiculous" system of competitive examinations. One gets the impression that one is listening to a spokesman of a superior nazi culture who has no understanding of the institutions of another people, intellectual though it may be, as are the French. It may be noted that Professor Leriche was for years head of the department of surgery of the university of Strasbourg. This university will now undergo a reform according to the nazi pattern.

Overcrowding in University of Oslo

Matriculation in the faculty of medicine of the University of Oslo has been such as to overtax lecture and training room facilities. Two hundred and sixty medical students, especially registrants for upper clinical courses, could not be accommodated. A number of German universities, such as Breslau, Leipzig, Freiburg and Erlangen, were opened to these students.

Smoking by Female Technicians

Smoking by female technicians is animadverted on in a recent article in the *Female Technical Assistant*. The increasing use of tobacco with exposure to possible damage due to nicotine, it is pointed out, does not represent cooperation with the objectives for which the medical profession and the health authorities are striving.

Police Order Regarding Abortifacients

A recent police order dealing with methods and means of preventing pregnancy and inducing abortion gives the authorities the power to proceed against those engaged in the manufacture, advertising and use of the most common abortifacients as well as against contraceptives detrimental to health.

Blood Donor Center

A blood donor center has been organized in the Auguste-Victoria Hospital in Berlin. Suitable blood donors may be obtained by telephonic inquiry. The charge for individual service is 3 reichsmarks.

Marriages

CLIFTON JENNINGS DERRICK to Miss Elizabeth Russell McKenzie, both of West Palm Beach, Fla., in February.

BERLIN FRANCIS BARHAM to Miss Nancy E. McNeely, both of Winston-Salen, N. C., at Cooleemee in February.

RICHARD C. WOODSON to Miss Catherine Wall, both of Birmingham, Ala., in St. Augustine, Fla., February 8.

JOHN WILLIAM THURMOND, Augusta, Ga., to Miss Dora Elisabeth Tarver in Aiken, S. C., in March.

HOWARD WALTER BAKER, Philadelphia, to Miss Anna Marie Springer of Phoenixville, Pa., February 22.

WILLIAM H. FRIZELL to Miss Margaret Alexander, both of Brookhaven, Miss., in Meridian, March 16.

BENJAMIN FRANKLIN LOUNSBURY to Miss Elizabeth Shuman, both of Oak Park, Ill., in March.

JOHN FRANCIS REGISTER to Miss Margaret Lucette Brewer, both of Greensboro, N. C., February 15.

ROBERT F. SLOTTERBECK, Toledo, Ohio, to Miss Gertrude Cole of Washington, D. C., March 3.

EDWIN LAWRENCE KENDIG JR., Richmond, Va., to Miss Emily Parker of Appalachia in March.

JAMES B. HICKS, Gadsden, Ala., to Miss Dagny Magnhild Everson of Elliott, Mo., in February.

DAVID R. WEILL JR., Chattanooga, Tenn., to Miss Eva Ada Winkler in New York, March 2.

ALSTON CALLAHAN, Vicksburg, Miss., to Miss Eivor Holst of San Francisco, February 23.

HAIG CARAFETYAN to Miss Letitia Ingram Belknap, both of New York, February 15.

AARON W. NEWTON to Miss Marie C. Benson, both of Cleveland, in March.

BENJAMIN J. STEVENSON, Sparta, Ill., to Miss Nora Pheglcy of Modoc recently.

Deaths

Claude Thomas Wolfe ● Louisville, Ky.; Kentucky School of Medicine, Louisville, 1907; clinical professor of ophthalmology at the University of Louisville School of Medicine; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served during the World War; member of the staffs of the Norton Memorial Infirmary, Louisville City and Kentucky Baptist hospitals and St. Joseph Infirmary; consulting ophthalmologist at Kentucky School for the Blind; aged 57; died, April 9.

Jefferson Davis Bloom, New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1886; professor of diseases of children during the years 1890, 1891 and 1892 at the New Orleans Polyclinic; fellow of the American College of Surgeons; consultant and honorary member of the staff of the Hotel Dieu, Sisters' Hospital; aged 79; died, March 21, of aspiration pneumonitis and chronic myocarditis.

Denis Roscoe Wolff ● Greensboro, N. C.; Jefferson Medical College of Philadelphia, 1918; fellow of the American College of Surgeons; served during the World War; on the staffs of St. Leo's Hospital, L. Richardson Memorial Hospital and Piedmont Memorial Hospital; aged 44; died, March 23, in St. Anthony Hospital, St. Petersburg, Fla., of regional ileitis.

Walter F. Enfield, Bedford, Pa.; Medico-Chirurgical College of Philadelphia, 1894; member of the Medical Society of the State of Pennsylvania; at one time president of the Bedford County Medical Society; in 1923 member of the House of Delegates of the American Medical Association; aged 69; died, April 11, of carcinoma of the pancreas.

Walter Herndon Nelson, Silverton, Colo.; University of Texas School of Medicine, Galveston, 1935; member of the Colorado State Medical Society; on the staff of the Mercy Hospital, Durango, from 1937 to 1939; aged 35; died, March 13, in the Colorado General Hospital, Denver, of coronary thrombosis and cerebral embolism.

Elisabeth A. Ryder, Devon, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1891; member of the Medical Society of the State of Pennsylvania; part owner and superintendent of the Alcluyd Hospital; aged 76; died, March 14, in the Bryn Mawr (Pa.) Hospital of hypertensive cardiovascular disease.

Arnold Edgar Robison ● Provo, Utah; University of Nebraska College of Medicine, Omaha, 1921; past president and secretary of the Utah County Medical Society; served during the World War; formerly city physician; aged 46; on the staff of the Utah Valley Hospital, where he died, March 23.

Edwin Bannister Forbes ● Detroit; Harvard Medical School, Boston, 1898; Medizinische Fakultät der Universität Wien, Austria, 1899; served during the World War; formerly county physician; aged 66; died, April 15, in the Harper Hospital of bronchopneumonia and carcinoma of the pharynx.

William O'Gorman Quinby ● Newark, N. J.; Columbia University College of Physicians and Surgeons, New York, 1900; member of the American Academy of Ophthalmology and Otolaryngology; served during the World War; aged 64; died, March 24, of coronary occlusion and arteriosclerosis.

William Thomas McConville, Honesdale, Pa.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1895; member of the Medical Society of the State of New York; served during the World War; aged 69; died, March 18, in a hospital at Goshen, N. Y.

Llewellyn Powell, Alexandria, Va.; George Washington University School of Medicine, Washington, D. C., 1904; member of the Medical Society of Virginia; city coroner; served during the World War; on the consulting staff of the Alexandria Hospital; aged 62; died, March 13.

Henry John Heusinkveld ● Fulton, Ill.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1883; an Affiliate Fellow of the American Medical Association; for many years member of the board of education, and health officer; aged 81; died, March 13.

Thomas Wilson Crowder, Sherman, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1893; fellow of the American College of Surgeons; on the staff of St. Vincent's Hospital; aged 68; died, April 6, of gastric hemorrhage and heart disease.

Pearl Suvilla Waters, Patton, Calif.; Pulte Medical College, Cincinnati, 1910; member of the California Medical Association; on the staff of the Patton State Hospital; aged 64; died, March 7, in St. Joseph Hospital, Orange, of carcinoma of the cervix.

Ernest Robertson ● Beaumont, Texas; University of Texas School of Medicine, Galveston, 1925; served during the World War; aged 41; on the staffs of St. Therese Hospital and the Hotel Dieu Hospital, where he died, March 19, of cerebral hemorrhage.

John Horatio Dorsey, Grantsville, Md.; University of Maryland School of Medicine, Baltimore, 1885; veteran of the Spanish-American War; at one time a member of the state legislature of Minnesota; aged 89; died, April 10, of chronic myocarditis.

Edward Waddell Hooper, Humboldt, Kan.; Drake University Medical Department, Des Moines, Iowa, 1898; member of the Kansas Medical Society; served during the World War; aged 64; died, March 7, of carcinoma of the stomach and liver.

Albert Caleb Griffin, Whitestone, N. Y.; Albany Medical College, 1880; College of Physicians and Surgeons, medical department of Columbia College, New York, 1881; aged 85; died, February 20, of coronary thrombosis and arteriosclerosis.

Clifford Lombard Crittenden, Detroit; Michigan College of Medicine and Surgery, Detroit, 1905; aged 69; on the staffs of the Harper Hospital and the Grace Hospital, where he died, April 6, of bronchopneumonia and cirrhosis of the liver.

John Sherman Sprague, Indianapolis; Medical College of Indiana, Indianapolis, 1905; member of the Indiana State Medical Association; on the staff of the Veterans Administration Facility; aged 63; died, March 27, in St. Joseph Hospital.

Jonathan Arthur W. Burgess ● Iowa Falls, Iowa; State University of Iowa College of Medicine, Iowa City, 1895; on the staff of the Ellsworth Municipal Hospital; aged 72; died, March 26, in Chicago of coronary thrombosis.

Marie Lois Grote, Topeka, Kan.; Northwestern University Woman's Medical School, Chicago, 1894; formerly on the staff of the Lincoln (Neb.) State Hospital; aged 79; died, February 17, of arteriosclerosis and bronchopneumonia.

Frank Hinkley, Brightwaters, N. Y.; Albany Medical College, 1898; member of the Medical Society of the State of New York; for many years on the staff of the Central Islip (N. Y.) State Hospital; aged 66; died, March 10.

Robert Hebenstreit, Buffalo; University of Buffalo School of Medicine, 1872; member of the Medical Society of the State of New York; aged 90; died, March 25, of bronchopneumonia and carcinoma of the bladder.

James Burrow Edwards, Fort Dodge, Kan.; Hospital College of Medicine, Louisville, Ky., 1898; member of the Kansas Medical Society; served during the World War; aged 73; died, April 4, of Parkinson's disease.

William Ashford Sampson, San Francisco; Hahnemann Medical College of the Pacific, San Francisco, 1909; served during the World War; aged 57; died, March 11, in the Veterans Administration Facility, Palo Alto.

Arthur Whitaker Belting ● Trenton, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1903; formerly secretary of the state board of medical examiners; aged 62; died, March 24, of coronary thrombosis.

Harry Allen Sadden ● Rochester, N. Y.; Syracuse University College of Medicine, 1908; served during the World War; on the staff of the Rochester General Hospital; aged 59; died, March 22, of acute leukemia.

George Peter Sackrider, Owosso, Mich.; Detroit College of Medicine, 1904; member of the Michigan State Medical Society; served during the World War; aged 66; died, March 11, of coronary occlusion.

Kenneth Earl Shaweker, Dover, Ohio; University and Bellevue Hospital Medical College, New York, 1914; fellow of the American College of Surgeons; served during the World War; aged 52; died, March 20.

Liselotte Herz, New York; Medizinische Fakultät der Universität Wien, Austria, 1938; intern at the Montefiore Hospital for Chronic Diseases; aged 26; died, March 18, of an overdose of sleeping tablets.

George Arthur Huntley, Branson, Mo.; University of Vermont College of Medicine, Burlington, 1897; for many years a medical missionary in China; aged 75; died, March 2, of myocarditis and influenza.

Adolph George Rave, Hicksville, N. Y.; Kentucky School of Medicine, Louisville, 1893; member of the Medical Society of the State of New York; aged 70; died, March 27, of arteriosclerosis and heart disease.

Eber Dunbar Kanaga, Palm Springs, Calif., University of Michigan Department of Medicine and Surgery, Ann Arbor, 1908; member of the Washington State Medical Association; aged 63; died, March 31.

Ernest Choquette, St. Hilaire Village, Que., Canada; M.B., Laval University Faculty of Medicine, Quebec, 1884; M.D., Laval University Medical Faculty, Montreal, 1886; aged 78; died, March 29.

Fred Eli Redman, Washington, D. C.; Northwestern University Medical School, Chicago, 1907; served during the World War; on the staff of the Veterans Administration; aged 58; died, March 28.

John Lachlan MacIsaac, Antigonish, N. S., Canada; Baltimore Medical College, 1907; fellow of the American College of Surgeons; surgeon to St. Martha's Hospital; aged 71; died, March 25.

Ephym Efrem Syrkin, Brooklyn; Universität Bern Medizinische Fakultät, Switzerland, 1916; executive director of the Beth Moses Hospital; aged 52; died, March 26, of carcinoma of the larynx.

Oscar La Fayette Berdan, Strathroy, Ont., Canada; Trinity Medical College, Toronto, 1889; medical health officer of Strathroy; served during the World War; aged 72; died, March 3.

Harden T. Leach, Elston, Mo.; Washington University School of Medicine, 1896; member of the Missouri State Medical Association; aged 75; died, March 30, of arteriosclerosis.

Jesse M. Yonan, Chicago; Rush Medical College, Chicago, 1895; member of the Illinois State Medical Society; aged 73; died, March 13, of cerebral hemorrhage, arteriosclerosis and arthritis.

Harry Nalley, Mount Rainier, Md.; University of Maryland School of Medicine, Baltimore, 1900; member of the Medical and Chirurgical Faculty of Maryland; aged 64; died, February 7.

Israel Louis Feinberg, New York; University of the City of New York Medical Department, 1893; aged 70; died, April 13, in the Knickerbocker Hospital of cerebral hemorrhage.

James Walter Park, Kaufman, Texas; Louisville (Ky.) Medical College, 1880; member of the State Medical Association of Texas; aged 85; died, March 6, of coronary thrombosis.

Benjamin Franklin Babb, Ivor, Va.; University of Maryland School of Medicine, Baltimore, 1892; aged 76; died, March 31, in the Lakeview Hospital, Suffolk, of heart disease.

Abram M. Miller, Hyndman, Pa.; Baltimore Medical College, 1905; member of the Medical Society of the State of Pennsylvania; aged 71; died, March 4, of coronary thrombosis.

Thomas B. Perry, Miami, Fla.; College of Physicians and Surgeons, Baltimore, 1885; veteran of the Spanish-American War; aged 77; died, March 8, of acute dilatation of the heart.

William C. Watkins, Oconto, Wis.; Baltimore Medical College, 1905; member of the State Medical Society of Wisconsin; served during the World War; aged 61; died, March 19.

William H. Smith ● Cincinnati; Pulte Medical College, Cincinnati, 1896; on the staff of the Bethesda Hospital; aged 66; died, March 22, in Miami, Fla., of coronary thrombosis.

James Joseph Moorhead ● Terre Haute, Ind.; Rush Medical College, Chicago, 1895; on the staff of St. Anthony's Hospital; aged 78; died, March 16, of chronic myocarditis.

Archibald William Moss ● Binghamton, N. Y.; Long Island College Hospital, Brooklyn, 1921; aged 45; died, March 16, in Our Lady of Lourdes Hospital of cerebral embolism.

David Thomas Percy, Arlington, Mass.; Harvard Medical School, Boston, 1891; member of the New England Pediatric Society; aged 72; died, March 27, of coronary thrombosis.

John Robert Hendry, Detroit; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1922; aged 45; died, March 4, in the Harper Hospital of heart disease.

John Hunton Moss ● Binghamton, N. Y.; Jefferson Medical College of Philadelphia, 1914; served during the World War; aged 55; died, March 30, of coronary occlusion.

Rozilla Crofford, Burr Oak, Mich.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1886; Eclectic Medical Institute, Cincinnati, 1888; aged 80; died, March 31.

William Dalton Walker, Seattle; St. Louis University School of Medicine, 1903; aged 63; died, March 19, of pulmonary hemorrhage and dissecting aortic aneurysm.

James Taylor Walker, Richmond, Va.; College of Physicians and Surgeons, Baltimore, 1886; member of the Medical Society of Virginia; aged 81; died, March 12.

Robert Henry Montgomery, Detroit; Meharry Medical College, Nashville, Tenn., 1933; aged 34; died in March in the Grace Hospital of rheumatic heart disease.

John Henry Sullivan, Worcester, Mass.; Dartmouth Medical School, Hanover, N. H., 1894; aged 71; died, March 17, of arteriosclerosis and heart disease.

Stephen Summers Hanson, Haney, B. C., Canada; Western University Faculty of Medicine, London, Ont., 1893; aged 71; died, March 20, in Essondale.

John M. Fadeley, Point Pleasant, W. Va.; Maryland Medical College, Baltimore, 1905; county coroner; aged 63; died, April 10, of coronary thrombosis.

Richard Herrick ● Wyanet, Ill.; Eclectic Medical Institute, Cincinnati, 1891; served during the World War; aged 76; died, March 25, of chronic myocarditis.

George C. Merriam ● Empire, Ala.; Atlanta (Ga.) College of Physicians and Surgeons, 1902; aged 66; died, March 22, in the Norwood Hospital, Birmingham.

Chauncey Wyckoff Howell ● Grinnell, Iowa; Northwestern University Medical School, Chicago, 1911; aged 54; died, March 10, of myocarditis.

George Alfred Hull, New York; New York Homeopathic Medical College and Hospital, New York, 1889; also a dentist; aged 71; died, March 18.

William Burchett Page, Granville, Tenn.; University of Nashville Medical Department, 1871; aged 90; died, March 7, of cerebral hemorrhage.

Carlyle Raymond Jones, Atlantic, Iowa; John A. Creighton Medical College, Omaha, 1908; aged 59; died, March 8, of pulmonary embolus.

Penrose Harold Marquette, Shamokin, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1925; aged 41; died, March 23.

Edgar Holm ● Eureka, Calif.; Northwestern University Medical School, Chicago, 1903; aged 63; died, March 9, of coronary embolism.

Franklin May Sanders, Adamsville, Tenn. (licensed in Tennessee in 1926); served during the World War; aged 53; died, March 16.

Charles Benjamin Abbott, Hillsboro, N. H.; Dartmouth Medical School, Hanover, 1902; aged 68; died, March 24, of heart disease.

Silas Grant Wertz, Wilkinsburg, Pa.; Jefferson Medical College of Philadelphia, 1895; aged 72; died, March 18, in Pittsburgh.

Colin Reed Weirich, Bridgeville, Pa.; Jefferson Medical College of Philadelphia, 1882; aged 83; died, March 11, of lobar pneumonia.

Peter Radebaugh, Sturgis, Mich.; Miami Medical College, Cincinnati, 1887; aged 87; died, March 23, of influenza and prostatitis.

William S. Windsor, Climax Springs, Mo.; University of Maryland School of Medicine, Baltimore, 1890; aged 79; died, March 14.

George John Ott ● Boston; Albany (N. Y.) Medical College, 1894; aged 73; died, March 29, of a staphylococcic infection.

James Hutchinson Bartley, Zillah, Wash.; Rush Medical College, Chicago, 1900; aged 69; died, February 12, of heart disease.

Lee Zuber, Sweet Home, Ark.; University of Arkansas School of Medicine, Little Rock, 1901; aged 75; died, March 3.

William M. Houghton, Floydada, Texas (licensed in Texas, under the Act of 1907); aged 73; died in March.

George W. Sisler, Tulsa, Okla. (licensed in Oklahoma in 1924); aged 77; died, March 23, of coronary thrombosis.

Edgar Browning, Sherbrooke, Que., Canada; M.R.C.S., England and L.R.C.P., London, 1887; died, February 5.

William Y. Corry, Vancouver, B. C., Canada; Detroit College of Medicine, 1897; aged 72; died, February 16.

Harry E. Mechling, Louisville, Ky.; Hospital College of Medicine, Louisville, 1900; aged 71; died in March.

Harley Parker, Chicago; Hering Medical College, Chicago, 1895; aged 66; died, March 3.

Bureau of Investigation

KOCH CANCER "CURE" AND THE CANADIAN CANCER COMMISSION

THE JOURNAL has frequently commented on the Koch cancer treatment. The Bureau of Investigation is in receipt of a letter dated April 2 addressed to a physician in Texas, from the Koch Laboratories of Detroit, carrying the signature "Wm. F. Koch, Ph.D., M.D.," which reads as follows:

"The CANADIAN CANCER COMMISSION appointed by the ONTARIO Government has compiled a splendid series of scientific PROOFS of the EFFICACY of the KOCH TREATMENT in curing advanced CANCER.

"In order to make this presentation available to interested physicians it is reproduced verbatim in a four hundred page book which is distributed for one dollar to cover printing and mailing costs.

"To give a practical conception of the clinical and scientific aspects of this work our book on natural immunity will be sent to you for the asking.

"Aside from humanitarian interest you will find that these books offer you a means of increasing your efficiency and income."

Of interest in connection with the claim made in the first paragraph is a clipping taken from the Toronto *Daily Star* for March 19, which deals with a report of the Ontario Cancer Commission, pointing out that this is the third report and that it has nothing to add to its November report in which it expressed the opinion that the investigation of "Ensol," the discovery of Dr. Hendry Connell of Kingston, Ont., "be continued," that they would be willing to consider "Essiac," sponsored by Miss Rene Caisse of Bracebridge, "if furnished with formula and samples," and continues as follows:

> "Or Glyoxylide, sponsored by Dr. David Arnott of London, Ont., the Commission reports it 'is still hopeful that progress may be made . . . And thinks it desirable to defer any review of the evidence before it to date or the expression of any opinion until it either has the benefit of some laboratory study or it is finally successful in having an investigation made.'"

CEASE AND DESIST ORDERS

Abstracts of Certain Federal Trade Commission Releases

The work of the Federal Trade Commission, in helping to protect the public against misrepresentation or fraud in the medical as well as other fields, has been greatly extended by the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act. The Food, Drug and Cosmetic Act of 1938 added to the Food and Drug Administration's control of the advertising claims and statements made on the labels of medicines or on the carton or in the accompanying leaflet, whereas what might be termed collateral advertising, that which appears in newspapers and magazines and over the air, comes more actively under the purview of the Federal Trade Commission, by virtue of the Wheeler-Lea Amendment.

THE JOURNAL has at various times commented on the activities of the Federal Trade Commission in this connection, even before the Wheeler-Lea Amendment gave it its added rights. In some cases the Commission may accept from the person or concern involved a **stipulation** that the objectionable practices or claims cited will be discontinued. In other cases the Commission issues what is known as a Cease and Desist Order, in which the individual, manufacturer or distributor cited is ordered to cease and desist from practices which have been declared objectionable.

Abstracts of some of the orders issued during 1940 follow:

Clito Products.—There are two of these, designated as "Clito Emmenagogue Capsules" and "Rayo De Sol" and put out by a Rene P. Balditt, trading as the Clito Company, San Antonio, Texas. The Federal Trade Commission's investigation revealed that Rayo De Sol is not, as represented, a cure for cataracts, cloudy vision, film carnosity, ulcers and inflammation of the eyes, and that Clito Emmenagogue Capsules are not a safe and competent treatment for delayed menstruation. On Oct. 28, 1940, the Commission ordered Balditt to cease making these misrepresentations and to discontinue advertisements that fail to reveal that Clito Emmenagogue Capsules may cause gastro-intestinal disturbances and excessive congestion and hemorrhage of the pelvic organs and, in case of pregnancy, may cause uterine infection and blood poisoning.

Concentra.—A Chicago concern operating under the name Jean Ferrell, Inc., advertised this product as a highly concentrated food, safe for use and (with the addition of liquids) as constituting a balanced diet capable of replacing the ordinary diet. It was also claimed to supply deficiencies of the body, to correct overweight and underweight and to eliminate poisons from the kidneys because of its gravel root content, and poisons in general from the body by action of its rhubarb content. The Federal Trade Commission on March 15, 1940, ordered the concern to discontinue these representations, charging that they were exaggerated and untrue, that the preparation is not a food and that because of its high content of rhubarb, it is a drug and not safe to use. Jean Ferrell, Inc., was also ordered to cease disseminating advertisements of Concentra which fail to reveal that continued use of the preparation over a long period would cause excessive purgation and result in serious injury to the health of the user. Another federal agency, the Food and Drug Administration, prosecuted Jean Ferrell, Inc., for misrepresentation on the ground that the claims made in or on the trade package of Concentra violated the *Food and Drugs Act* in fraudulently representing, among other things, that this nostrum was a food, whereas it consisted essentially of a drug. This drug was reported by government chemists to be rhubarb root. Their analysis also disclosed the presence of some dried extractive material, soya bean tissues and Irish moss tissues. This case, designated as *Notice of Judgment 30666*, November 1939, was reported in THE JOURNAL, May 4, 1940, page 1825.

Dermagell.—This product, originally put out by Research Associates, Inc., Washington, D. C., was later taken over by Dermagell, Inc., of the same city. It was claimed to be "a 3-purpose Cleansing Cream and Shampoo—so efficient—so utterly different from anything heretofore obtainable that authorities proclaim it 'the discovery of the century' . . . soothes and heals as it penetrates innermost recesses of the tender pores without unpleasant reaction . . . actually protects your skin . . . prevents pores many skin disorders." The Federal Trade Commission, on May 16, 1940, declared that this product is not substantially different from any other preparations or soaps designed for similar use, that it possesses no special soothing or healing properties and that other claims made for it were false and misleading. It therefore ordered that such misrepresentations be discontinued in the advertising.

Faid.—This item is put out by the Chapman Health Products Company of Cleveland, which also put out "N. A. R. Tablets." The tablets were represented as a cure or remedy for rheumatism, neuritis and arthritis, and "Faid," also known as "Daintee," as a cure or remedy and a safe, scientific treatment for obesity. The latter, according to the Federal Trade Commission, contained powdered extract of phytolacca berries, sodium biborate, berberine hydrochloride, apocynoid (?) and desiccated thyroid, in quantities sufficient to cause serious and irreparable injury to health if taken under customary and usual conditions or under those prescribed in the advertising. The composition of the N. A. R. Tablets was not given. The Federal Trade Commission, on May 10, 1940, declared that the representations made for these two products were unwarranted and ordered them discontinued.

Grape Cure for Cancer.—This treatment was exploited by one Johanna Brandt in her book "The Grape Cure," distributed by a Jessie F. Springer, operating as the Harmony Centre of New York. The Federal Trade Commission objected to this book on the ground that it represented that Johanna Brandt had cured herself of cancer through the use of the system of treatment described therein, which is based on the use of grapes, and that this treatment would cure cancer and practically all other human afflictions. The advertising itself contained objectionable representations, such as that most diseases originate in the intestine and are caused by poisons due to uneliminated waste; that grapes dissolve mucus, that those who develop malignant growths have in most cases been suffering from constipation; that salt, inorganic drugs and "patent medicines" cause cancer and that the system or method of treatment outlined in the book will restore one's health. On March 15, 1940, the Commission ordered that such misrepresentations be discontinued. The American Medical Association's records indicate that in 1928 Johanna Brandt, who claimed to have come from South Africa the previous year, was herself running the Harmony Healing Centre in New York, which concern was charged by state officials with practicing medicine without a license. Soon afterward one F. W. Collins, calling himself "dean" of the First National University of Naturopathy, Newark, N. J., announced that his institution had become the headquarters of the "Centre." Evidently the concern later was reopened in New York by Jessie Springer, who capitalized on the "grape cure" by propaganda by advertising that it had grape juices and grape concentrates for sale, as well as various "health books." The authors of some of these books were readily recognized as quacks or food faddists.

Nu-Myst.—This nostrum, put out by the Forson Laboratories, Inc., New York, was described by the Federal Trade Commission as "a liquid composed of common ingredients prescribed by physicians for relieving 'colds,' and containing menthol, camphor, thymol, oil of pine, eucalyptol, benzyl benzoate and aromatics, with an alcohol base of 87 per cent." The Commission charged that the Forson concern—through radio broadcasts and newspaper and magazine advertisements—falsely represented that its product would bring speedy relief to sufferers from colds, hay fever, rose fever, asthma and other nasal and bronchial disorders. The Commission pointed out that the disorders named, except colds, are grouped under the so-called allergies, the causes of which are manifold, and since there are so many causes it is impossible for a formula such as "Nu-Myst" to bring relief from any of these conditions. On April 14, 1940, therefore, the Commission ordered the Forson people to cease and desist from representing that their preparation will destroy or prevent the growth of bacteria; that it is a cure or remedy for colds, whooping cough, hay fever, rose fever or asthma or that it is an effective treatment for relief of these ailments beyond such temporary relief as may be afforded by the temporary allaying of local irritation.

Medical Examinations and Licensure

COMING EXAMINATIONS

BOARDS OF MEDICAL EXAMINERS

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, May 24, page 2425.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, June 23-25. Part III. Various centers, June or July. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written. Part I.* Various centers, Nov. 1. Final date for filing application is Aug. 4. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York City.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written.* Nov. 3. Final date for filing application is Sept. 23. *Oral.* Dec. 12-13. Final date for filing application is Nov. 8. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* June, in advance of the meeting of the American Medical Association. *Written.* Oct. 20. Final date for filing application is Sept. 1. Sec., Dr. William S. Middleton, 1201 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Philadelphia, June 6-7. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I. Group B.* Jan 3. *Oral. Part II. Groups A and B.* Atlantic City, May or June. Final date for filing application is 90 days in advance of the examination. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* New York, June 2; Portland, July 15; Chicago, Oct. 18. *Written.* March 7, 1942. Sec., Dr. John Green, 6830 Waterman Ave. St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Washington, January. Final date for filing application is Nov. 1. Sec., Dr. Guy A. Caldwell, 1640 State St., New Orleans, La.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 16-18. Final date for filing application is July 1. Sec., Dr. W. P. Wherry, 1509 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Boston, Oct. 7-8, immediately following the annual meeting of the American Academy of Pediatrics. *Written.* Locally, Aug. 22. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF RADIOLOGY: *Oral. All groups.* Cincinnati, Sept. 19-21. Final date for filing application is Aug. 1. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S. W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: Chicago, February. Final date for filing application is three months before date of examination. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Pennsylvania January Report

The Pennsylvania State Board of Medical Examiners reports the written and practical examination for medical licensure held at Philadelphia, Jan. 7-11, 1941. The examination covered 5 subjects and included 50 questions. An average of 75 per cent was required to pass. Forty-nine candidates were examined, 47 of whom passed and 2 failed. Six physicians were licensed by reciprocity and 1 physician so licensed by endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
College of Medical Evangelists		(1940)	1
George Washington University School of Medicine		(1938)	1
University of Chicago, The School of Medicine		(1939)	1
Louisiana State University School of Medicine		(1939)	1
Johns Hopkins University School of Medicine		(1939)	1
Harvard Medical School		(1938)	1
University of Michigan Medical School		(1936)	1
St. Louis University School of Medicine		(1939)	1
Washington University School of Medicine		(1937)	1
Creighton University School of Medicine		(1939)	1
Cornell University Medical College		(1935)	1
New York University College of Medicine		(1937)	1
Western Reserve University School of Medicine		(1936)	1
Hahnemann Med. College and Hosp. of Philadelphia		(1939, 9)	9
Temple University School of Medicine		(1936), (1937), (1938, 2), (1939, 3)	7
Univ. of Pennsylvania School of Medicine		(1936), (1938, 2)	3
University of Pittsburgh School of Medicine		(1939, 2)	2
University of Tennessee College of Medicine		(1939)	1
Medical College of Virginia		(1938)	1
University of Virginia Department of Medicine		(1938)	1
Marquette University School of Medicine		(1940)	1
Dalhousie University Faculty of Medicine		(1939)	1
Queen's University Faculty of Medicine		(1937)	1
University of Toronto Faculty of Medicine		(1923), (1936)	2
McGill University Faculty of Medicine		(1937)	1
Medizinische Fakultät der Universität Wien		(1919, 2)	2
Deutsche Universität Medizinische Fakultat, Prag		(1936)	1
Université de Lausanne Faculté de Médecine		(1930)	1

School	FAILED	Year Grad.	Number Failed
Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn		(1934)	1
Regia Università di Napoli Facoltà di Medicina e Chirurgia		(1938)	1

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Georgetown University School of Medicine		(1932)	Iowa
Loyola University School of Medicine		(1938)	Illinois
University of Michigan Medical School		(1936)	Michigan
University and Bellevue Hospital Medical College		(1930)	New York
Hahnemann Med. College and Hospital of Philadelphia		(1934)	New Jersey
Medical College of Virginia		(1929)	W. Virginia

School	LICENSED BY ENDORSEMENT	Year Grad.
Yale University School of Medicine		(1937)

Arizona January Report

The Arizona State Board of Medical Examiners reports the written examination for medical licensure held at Phoenix, Jan. 7-8, 1941. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. One candidate was examined and passed. One physician was licensed to practice medicine by reciprocity and 1 physician so licensed by endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Kansas School of Medicine		(1938)	79.5

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Stanford University School of Medicine		(1937)	California

School	LICENSED BY ENDORSEMENT	Year Grad.
Woman's Medical College of Pennsylvania		(1935)

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Osteomyelitis Attributed to Force Used by Physician in Restraining Patient.—As the patient, a boy of 7 or 8 years of age, was being wheeled into the operating room preparatory to the removal of his adenoids by the defendant physician he became frightened and kicked a nurse in the stomach. The physician seized him by his arms and held him down on a table until the nurse administered ether. The following day finger marks were visible on the boy's skin at the upper end of the right humerus. About five days after the operation the child began to suffer from osteomyelitis of the upper right humerus. Attributing the osteomyelitis to the physician's grasping of the child's arm in the operating room, two suits were instituted against the physician, one by the child's father and the other on behalf of the child. The two suits were apparently consolidated for trial.

At the trial medical experts, apparently called by the physician, testified that although trauma with the presence of an infectious germ is an adequate cause for osteomyelitis, the source of osteomyelitis in the minor must be sought in some occurrence prior to the date of the operation, by which time the trouble was already in the process of development. To controvert this testimony, the plaintiff's called a general practitioner of medicine who, according to his testimony, in thirty-one years of practice had treated more than a hundred patients with osteomyelitis. This physician testified that "trauma with the presence of an infectious organism in the system would be an adequate cause of osteomyelitis at the place of the trauma; that with adenoids an infectious organism would be present; and that the grasping of the boy's arm and forcing him down upon a table with sufficient force to leave finger marks would be adequate cause for the 'stretching of the capsule in the boy's arm at the glenoid fossa,'" which condition was indicated in a roentgenogram that had been taken of the child. The court then refused to permit the witness to answer three hypothetic questions, one of which, in effect, would have called for his opinion as to whether or not the grasping of the boy's arms in the operating room was an adequate cause of the osteomyelitis;

another as to what caused the osteomyelitis; and the third as to whether a force sufficient to leave marks on the arm would, if there was some stretching of the capsule, be sufficient to cause osteomyelitis. From verdicts in favor of the physician the plaintiffs, in effect, appealed to the Supreme Judicial Court of Massachusetts, Worcester, claiming the trial court erred in refusing to permit the witness to answer the questions referred to.

The testimony of the witness called by the plaintiffs as an expert that was permitted in evidence, said the Supreme Judicial Court, made plain to the jury that the violent grasping of the boy's arms under the circumstances might produce osteomyelitis. It was not error for the trial court to exclude the opinion of the witness as to whether the osteomyelitis existing five days after the operation was or could be so caused. In his discretion the trial court might decide that the physician in question was not sufficiently versed in osteomyelitis to make his opinion valuable to the jury since the qualifications of an expert are to be determined by the trial judge, and his judgment is seldom overturned. The verdicts of the jury in favor of the defendant were not, in the opinion of the court, tainted by any error of law and were accordingly affirmed.—*Carbonneau v. Lachance (two cases), 29 N. E. (2d) 696 (Mass., 1940).*

Malpractice: Release of Hospital as Bar to Action Against Physician.—The plaintiff's wife died, allegedly, from an overdose of paraldehyde, a narcotic administered for the purpose of producing "twilight sleep." The defendant, the attending physician, had prescribed the administration of 4 drachms (15 cc.) of the drug, but a nurse employed by the hospital gave the patient 4 ounces (120 cc.) instead. The plaintiff eventually made a settlement, in the amount of $1,900, with the hospital owner, the settlement being based on the theory that the death was due to the negligence of the nurse employed by the hospital. The plaintiff then sued the defendant physician for damages for the wrongful death of his wife. From a judgment for the defendant in the trial court, the plaintiff appealed to the Supreme Court of Florida.

The defendant contended that he and the hospital, if guilty at all, were guilty as joint tort feasors and that the release of the hospital owner barred the plaintiff from any further claims on account of his wife's death. The Supreme Court said that the theory of the release was that the death was caused by the hospital owner or her servant, the nurse who actually administered the drug, and that the theory of the present lawsuit was that the defendant physician was solely responsible for the death because he negligently prescribed the use of the drug and caused it to be administered. These theories were so inconsistent, held the court, that there could not be a recovery on both of them. Whether the hospital owner and the attending physician were joint or several tort feasors, continued the court, the law would not permit the plaintiff to treat them as several for the purpose of making a settlement with one, as was done here, and then treat them as joint for the purpose of an action at law against the other to recover for the same wrong. The judgment in favor of the defendant physician was therefore affirmed.—*Sands v. Wilson, 191 So. 21 (Fla., 1939).*

Workmen's Compensation Acts: Compensability of Diseases Contracted by Nurses and Interns.—In three cases which arose in New York, the question concerned the application of the workmen's compensation act to certain diseases contracted by nurses and interns in the course of their duties. In the Miller case, the plaintiff was a student nurse and became disabled as the result of tuberculosis alleged to have been contracted as a result of the nature of her employment. While the claimant was unable to name any particular patient suffering from tuberculosis whom she attended, the record disclosed that an examination made at the time she entered the service established that she had no symptoms of the disease. There was medical testimony to the effect, too, that the claimant became infected subsequent to her admission as a nurse. The supreme court, appellate division, third department, affirmed an award of compensation in favor of the nurse, but the Court of Appeals reversed the award and remanded the case to the industrial board for a further hearing on the ground that the evidence was insufficient to sustain the award. In the Waterman case, the supreme court, appellate division, third department, affirmed an award in favor of a nurse who contracted syphilis while caring for an infant suffering from congenital syphilis. In the Turitto case, the plaintiff was an intern who lost the sight of one eye because of gonorrheal ophthalmia contracted while attending a patient suffering from acute gonorrheal urethritis on whom an operation had been performed. The supreme court, appellate division, third department, affirmed the award of the industrial board in favor of the plaintiff.—*Miller v. City of New York et al., 14 N. Y. S. (2d) 680 (N. Y., 1939), 26 N. E. (2d) 821 (N. Y., 1940); Waterman v. Jamaica Hospital et al., 14 N. Y. S. (2d) 636 (N. Y., 1939); Turitto v. St. Mary's Hospital et al., 14 N. Y. S. (2d) 647 (N. Y., 1939).*

Dead Bodies: Disposal Must Not Offend Common Decency.—The aged sister of the equally aged defendant with whom she had lived died following a fall. The defendant dragged the corpse down into the basement, built up a roaring fire in the furnace and shoved it gradually into the flames. A neighbor noticed a heavy, dark smoke with a rather disagreeable odor pouring from the chimney of the defendant's house and reported that fact to the police. A police officer was later sent to the defendant's home to make an investigation. The defendant took the officer down into the basement, scraped the ashes out of the furnace and said "If you want to see her, there she is." Only a few bones were found. The defendant was subsequently convicted of indecently and unlawfully disposing of his sister's dead body "to the great indecency of Christian burial," and he appealed to the Supreme Judicial Court of Maine.

It was conceded that the defendant had not committed an offense covered by any specific statute, but the state contended that he was guilty of a crime at common law. Any disposal of a dead body, said the Supreme Judicial Court, which is contrary to common decency is a crime at common law. The court could not agree with the defendant's argument that, because cremation is now a well recognized method of disposing of dead bodies and is not contrary to common decency, the defendant's burning of the dead body of his sister was not a crime. As was stated in *Reg. v. Price*, 12 Q. B. D. 247, ". . . a person who burns instead of burying a dead body does not commit a criminal act, unless he does it in such a manner as to amount to a public nuisance at common law." In the present case the offense was not that the body had been burned but that it had been indecently burned "in such a manner that, when the facts should in the natural course of events become known, the feelings and natural sentiments of the public would be outraged." The judgment of conviction was therefore affirmed.—*State v. Bradbury, 9 A. (2d) 657 (Maine, 1939).*

Malpractice: Liability of Physician for Prenatal Injuries to Infant.—The plaintiff, a girl aged 11 years, by her mother as guardian ad litem brought suit against the defendant physician for injuries sustained by her prior to her birth. She claimed that, because of the alleged negligent application of "metal clamps and forceps" by the defendant to assist him in delivering her prior to her birth, her "brain cells and spine" had been seriously injured resulting in permanent paralysis. She based her right of action on section 29 of the Civil Code of California, which provides: "A child conceived, but not yet born, is to be deemed an existing person, so far as may be necessary for its interests in the event of its subsequent birth." The plaintiff's mother was not personally a party to the suit. The trial court upheld the defendant's demurrer and rendered judgment in his favor. The plaintiff then appealed to the district court of appeal, third district, California.

The district court could not agree with the defendant's contention that the word "interests," as used in the statute just quoted, is limited in its application to a child's right of inheritance or to its property rights and does not give the plaintiff the right to maintain an action for tort committed on her prior to her birth. The language of the statute, said the court, is as

clear and concise as the English language can make it, and there is nothing to indicate that the word "interests" is not used in its general sense of anything that is profitable or beneficial to the child. The court held, therefore, that the statute was broad enough to include both personal rights and property rights.

The defendant's further contention, that the statute should be construed to be merely a continuation of the common law with respect to the rights of an unborn child, likewise did not meet with the court's approval. At common law the great weight of authority does hold that an unborn child has no existence as a human being separate from its mother and that therefore it has no right of action for personal injuries inflicted on it prior to its birth by the wrongful act of another. But the California statute in question is diametrically opposed to that common law theory because it declares that under certain circumstances an unborn child shall be deemed "an existing person." Certainly such a radical change from the common law rule cannot be considered a continuation of such rule. Since this statute considers an unborn child an existing person, after its birth its parents, by authority of section 376 of the California Code of Civil Procedure, have the right to maintain an action in the child's behalf for injuries sustained by it through the wrongful act or neglect of another. Furthermore, even at common law a distinction has often been drawn between an unborn child whose lungs and other organs are fully developed, so that it would be capable of living separate and apart from its mother, and one which is less developed. The language of some of the court decisions indicate that an action might lie for injury to an unborn child if it were viable at the time of the injury. The court remarked that in the present case there was no doubt that the child was viable and capable of existence separate and apart from its mother at the time of the alleged injury. It was fully developed in every respect. The injuries were alleged to have occurred in the very process of delivering the child.

We do not suggest, said the court, that the defendant in the present case was guilty of malpractice. It may be true that he made no mistake in the delivery of the child. Even if he did, a mere mistake in the judgment of a physician does not constitute malpractice. It may be impossible for the plaintiff to prove satisfactorily that the defendant's conduct contributed in any degree to her unfortunate condition, but the mere fact that the assumed wrong is not readily susceptible of proof should not deprive the plaintiff of her right to pursue a remedy for that assumed wrong.

The district court, therefore, reversed the judgment for the defendant and directed the trial court to overrule the demurrer and permit the defendant to answer. On appeal by the defendant to the Supreme Court of California the opinion and judgment of the district court were affirmed.—*Scott v. McPheeters, 92 P. (2d) 678; 93 P. (2d) 562 (Calif., 1939).*

Dental Practice Acts: Revocation of License for Unlawful Advertising—When "Harsh and Unreasonable."—The defendant state board of registration and examination in dentistry of New Jersey on Jan. 4, 1939 formally charged the plaintiff, a licensed dentist, with having advertised in the Jan. 19, 1938 issue of the *Jersey Journal* "the prices and charges to be made for dental work . . . as well as the character and durability of said work" in violation of a New Jersey statute which prohibits advertising by dentists. The evidence showed that this was the only violation which the plaintiff had committed. After a hearing on a plea of guilty by the plaintiff, the board formally adopted a resolution, on March 24, 1939, revoking the plaintiff's license to practice dentistry. From the board's ruling the plaintiff appealed to the supreme court of New Jersey.

A New Jersey statute, said the supreme court, provides:

> The [supreme] court may reverse or affirm in whole or in part the finding or determination of the board *or pronounce such judgment on the evidence as shall be warranted.*

The court held that under this statute it had the right to review the board's action and pronounce such judgment as it saw fit. The plaintiff's only contention was that the ruling of the board should be reversed because the revocation of his license was too harsh and unreasonable a penalty. The board, on the other hand, contended that the penalty was justified because the plaintiff had twice been put on notice of the illegality of the act which he subsequently performed. In 1935, the United States Supreme Court, in *Semler* v. *Oregon State Board of Dental Examiners,* 294 U. S. 608, 55 S. Ct. 570, 79 L. Ed. 1086, upheld the constitutionality of a statute similar to that which the plaintiff violated. In 1937, the supreme court of New Jersey, in a case decided by it, specifically directed the attention of the dental profession to the United States Supreme Court's decision. The board argued, in effect, that in view of these decisions the plaintiff had been amply warned of the possible consequences of his conduct. The supreme court pointed out, however, that the particular New Jersey statute in question was not upheld by the New Jersey courts until October 1938, nine months after the plaintiff's acts, and that it was not until a year after the plaintiff's acts that the board commenced its proceedings against him. This delay indicated to the court that there must have been some doubt even in the minds of the members of the board as to the validity of the statute, although they too were aware of the prior decisions. The court also called attention to the fact that the evidence showed that the plaintiff had practiced dentistry for sixteen years and had enjoyed a good reputation in that profession. In view of that evidence, plus the fact that the defendant was guilty of but a single violation, and the additional fact that no other violator had been penalized greater than by a thirty day suspension of his license, the court concluded that the penalty fixed by the board was unreasonably harsh and severe. Accordingly, the order of revocation of the plaintiff's license was reversed and an order of six months suspension entered.—*Schwartz v. State Board of Registration and Examination in Dentistry, 15 A. (2d) 322 (New Jersey, 1940).*

Workmen's Compensation Acts: Chiropractic Adjustments as Medical Services.—The sole question before the Supreme Court of Michigan in this case was whether or not chiropractic adjustments constituted "medical services" within the meaning of the workmen's compensation act. In the opinion of the court they did. While a chiropractor is not permitted to use the term "doctor," "physician" or "surgeon," he is nevertheless in Michigan held to be engaged in the "practice of medicine," even though his practice covers only a very restricted part of the general field of that practice. The court reasoned that since chiropractic manipulation is within the meaning of "practice of medicine," it is also within the meaning of "medical services." In answer to arguments pointing out the dangers in compelling employees to submit to treatment from chiropractors rather than from licensed physicians, the court disavowed any intention of holding that employees could be compelled to accept chiropractic treatment.—*Green v. Rawlings et al., 287 N. W. 557 (Mich., 1939).*

Society Proceedings

COMING MEETINGS

American Medical Association, Cleveland, June 2-6. Dr. Olin West, 535 North Dearborn St., Chicago, Secretary.

American Association for the Study of Allergy, Cleveland, June 2-3. Dr. J. Harvey Black, 1405 Medical Arts Bldg., Dallas, Tex., Secretary.

American Association for Thoracic Surgery, Toronto, Canada, June 9-11. Dr. Richard H. Meade Jr., 2116 Pine St., Philadelphia, Secretary.

American Association of Medical Milk Commissions, Cleveland, June 1-2. Dr. Paul B. Cassidy, 2037 Pine St., Philadelphia, Secretary.

American Association on Mental Deficiency, Salt Lake City, June 20-24. Dr. E. Arthur Whitney, Washington Road, Elwyn, Pa., Secretary.

American Broncho-Esophagological Association, Cleveland, June 3. Dr. Paul H. Holinger, 1150 North State St., Chicago, Secretary.

American College of Chest Physicians, Cleveland, May 31-June 2. Dr. Paul H. Holinger, 500 North Dearborn St., Chicago, Secretary.

American Laryngological, Rhinological and Otological Society, Los Angeles, June 16-18. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

American Medical Women's Association, Cleveland, June 1-2. Dr. Etta Gray, 649 South Olive St., Los Angeles, Secretary.

American Neurological Association, Atlantic City, N. J., June 9-11. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.

American Ophthalmological Society, Hot Springs, Va., May 29-June 1. Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn., Secretary.

American Orthopedic Association, Toronto, Canada, June 9-12. Dr. Charles W. Peabody, 474 Fisher Bldg., Detroit, Secretary.
American Physiotherapy Association, Asilomar, Calif., July 13-18. Miss Evelyn Anderson, Stanford University, Calif., Secretary.
American Proctologic Society, Cleveland, June 1-3. Dr. William H. Daniel, 1930 Wilshire Blvd., Los Angeles, Secretary.
American Radium Society, Cleveland, June 2-3. Dr. William E. Costolow, 1407 South Hope St., Los Angeles, Secretary.
American Rheumatism Association, Cleveland, June 2. Dr. A. R. Shands, Dupont Institute, Wilmington, Del., Secretary.
American Society of Clinical Pathologists, Cleveland, May 29-June 2. Dr. A. S. Giordano, 531 North Main St., South Bend, Ind., Secretary.
Association for Research in Ophthalmology, Cleveland, June 3. Dr. Conrad Berens, 15 East 70th Street, New York, Secretary.
Idaho State Medical Association, Sun Valley, June 18-21. Dr. F. B. Jeppesen, 105 North 8th St., Boise, Secretary.
Maine Medical Association, York Harbor, June 22-24. Dr. Frederick R. Carter, 22 Arsenal St., Portland, Secretary.
Montana, Medical Association of, Great Falls, June 24-26. Dr. Thomas F. Walker, 206 Medical Arts Bldg., Great Falls, Secretary.
Ohio State Medical Association, Cleveland, June 3. Mr. C. S. Nelson, 79 East State St., Columbus, Executive Secretary.
Pacific Northwest Medical Association, Spokane, Wash., June 25-28. Dr. C. W. Countryman, 407 Riverside Ave., Spokane, Wash., Secretary.
Utah State Medical Association, Salt Lake City, June 12-14. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Thirteenth Annual Meeting, Held in Chicago, Nov. 1 and 2, 1940

The President, Dr. CHARLES A. DOAN, Columbus, Ohio, in the Chair

(Concluded from page 2432)

Immune Response in Drug-Treated Patients with Pneumococcic Pneumonia

DRS. LUTHER L. TERRY, LAWRENCE D. THOMPSON and JOSEPH C. EDWARDS, St. Louis: This report embraces observations on the presence of agglutinins, mouse protective power and the polysaccharide cutaneous test in 77 patients treated with type specific serum and sulfapyridine; 36 patients treated with sulfapyridine and pneumococcus antigen; 14 patients treated with sulfapyridine alone, and 2 patients who entered the hospital after the crisis and consequently received no specific therapy. These 129 patients were distributed over types I, II, III, IV, V, VII and VIII; 112 of them recovered; 17 died. Observations are presented also on 4 cases of type XIV pneumonia in which only agglutinin studies and polysaccharide cutaneous tests were done as the type XIV pneumococcus is usually avirulent for mice.

Specific polysaccharide cutaneous tests were performed and specimens were secured for determination of agglutinins and mouse protective tests before therapy, three hours after serum therapy when serum was given, twenty-four hours after the beginning of any therapeutic measure and at two to five day intervals thereafter during hospital stay. The tests were also performed a short time before death on those patients who died.

Conclusions: 1. The type specific polysaccharide cutaneous test is a more reliable aid in prognosis than the mouse protective titer or the agglutinin concentration of the patient's serum, especially in those patients receiving adequate amounts of serum. 2. A limited number of observations indicated that the type specific polysaccharide cutaneous test is not passively transferred. 3. The combination of pneumococcus antigen with sulfapyridine resulted in a higher percentage of positive type specific polysaccharide cutaneous reactions, in more positive agglutinin reactions and in a higher mouse protective power than were observed in the limited number of cases (12) when sulfapyridine was used alone. 4. Patients with type III pneumonia are in a class distinct from others. The immune response as gaged by the tests in this study are not stimulated to the same degree as in other types of pneumonia. This may account in part for the lack of good response to drug therapy in many type III infections. 5. Death does occur in certain cases in spite of antibody response apparently adequate as far as can be determined by the observations indicated.

Solubility Studies on Acetylsulfapyridine

DR. A. C. CURTIS and SIDNEY S. SOBIN, PH.D., Ann Arbor, Mich.: From the consideration of acetylsulfapyridine solubilities, hematuria (which may presage a dangerous or even fatal complication) during the course of sulfapyridine therapy should be both predictable and preventable. Sample urines and prepared solutions of varying *p*H and specific gravity were tested for acetylsulfapyridine solubility. Roughly, the solubility increased with the specific gravity and the degree of alkalinity. The increase in solubility with increasing specific gravity may be in part related to concentration of urea.

Clinically, hematuria developing in patients receiving sulfapyridine at the University Hospital invariably occurred with limited fluid intake and a considerable prerenal deviation of fluid, insufficient alkali to produce an alkaline urine and a tendency toward acidosis consequent on self-imposed restrictions of food. More rigorous attention to urinary alkalinity by means of alkali administration, water balance and an adequate intake of food in patients with this type of therapy should be the rule.

Preliminary studies on acetylsulfathiazole show that its behavior is essentially like that of acetylsulfapyridine.

Influence of Sulfathiazole, Sulfapyridine and Sulfanilamide on Experimental Infections in Mice

DR. MERLIN L. COOPER and H. M. KELLER, M.S., Cincinnati: All mice survived when fed, ad libitum, a complete diet containing 1 per cent of sulfathiazole two or more days before being inoculated with Shigella paradysenteriae Flexner. Ninety-five per cent of mice survived a minimum fatal dose of S. paradysenteriae Flexner when different groups of mice were given, three hours later, a single dose of 1 mg. by stomach tube of sulfathiazole, sulfapyridine, sulfanilamide and sulfamethylthiazole. Seventy-eight per cent survived 10 minimum fatal doses, 38 per cent survived 100 and 3 per cent survived 1,000 minimum fatal doses. Similar results were obtained with Shigella paradysenteriae Sonne and Shigella alkalescens. Bacterial counts every three hours on the abdominal fluid and tail blood of infected mice showed that the counts in the untreated mice increased rapidly up to the time of death. In the mice treated with one dose of 2 mg. of sulfathiazole three hours after injection of the bacteria, the counts increased until six hours after administration of the drug, then rapidly decreased, and the mice recovered.

Changes with Age in Embryonic Heart Action as Recorded in Micromoving Pictures

BRADLEY M. PATTEN, PH.D., Ann Arbor, Mich.: The subject matter for this talk has been selected from a series of studies carried out on embryos kept alive with the aid of specially constructed glass chambers and artificial nutrient mediums. By this method it is possible to keep the living heart under continuous observation for long periods and to study the changes in its activities which accompany its structural development. Inherent local differences in the rate of contraction and the direction of propagation of beat were recorded by means of micromoving pictures. By the use of three stage amplification, records were obtained showing the sequential appearance of first, a simple sinusoidal curve, then the ventricular and later the sinoatrial complexes of the electrocardiogram. Electrocardiograms of adult pattern were obtained from the embryonic heart before its nervous connections had been established and before any of the so-called conduction system became recognizable microscopically.

Visualization of the Pulmonary Artery During Its Embolic Obstruction

DRS. JOSEPH H. JESSER and GEZA DE TAKATS, Chicago: With a 25 per cent solution of sodium iodide, two hundred and sixty-three exposures were made in 48 dogs in various positions and at various intervals. The pattern of the vascular tree was studied before and after the production of massive and peripheral types of emboli. In massive pulmonary embolism, with total obstruction of the main pulmonary artery, not only the right side of the heart but the inferior vena cava and the hepatic veins were seen to be engorged. In the peripheral type of embolism, obstructing the blood supply of one lobe or even less pulmonary tissue, arterial spasm was demonstrated in other areas. Areas of localized emphysema, indicating incomplete bronchial obstruction, were visualized. The effect of papaverine on the pulmonary vascular bed was studied. The clinical significance of these studies was noted.

DISCUSSION

DR. GEZA DE TAKATS, Chicago: It has been shown by postmortem studies that patients will die an unexplained death with a small embolus in the lower lobes of the lungs without obstruction to the main artery. This is difficult to explain unless it is assumed that certain reflex changes originate from this embolus, either from the periphery or from the dilatation of the right side of the heart and particularly of the pulmonary artery itself. Pressor receptors have been shown to exist in the pulmonary artery. It is felt that if the pressure is raised in the pulmonary artery a depressor effect can be obtained in the systemic circulation. We have some experiments to show that a bronchial constriction occurs during pulmonary embolism which may be abolished by papaverine. This work shows that in addition to the bronchodilator effect of papaverine there is an effect on the vascular bed. On the basis of these studies we feel that the pulmonary vascular bed can constrict and dilate under nervous influence and that the effect of papaverine on the pulmonary embolism might be explained by the additional effect on the pulmonary vascular system. We are not convinced that papaverine is the optimal drug. We are hoping that a more potent and more effective vasodilator can be found.

DR. LOUIS N. KATZ, Chicago: Changes in caliber of the pulmonary tree demonstrated by Dr. Jesser's method may not be due to active dilatation of the pulmonary blood vessels but rather to a passive dilatation following increase in the intrapulmonary vascular pressure. Recently we have been studying the changes in blood pressure in the pulmonary arteries of unanesthetized dogs by use of a modification of the London cannula. With papaverine we found that pressure in the pulmonary artery goes up at the same time at which the systemic arterial pressure goes down. I wonder, therefore, whether the dilatation recorded by Jesser and de Takats may not be due to a passive phenomenon associated with an increase in pulmonary pressure. This is important in considering the use of papaverine in pulmonary embolism. It may be that the action of papaverine may be different when pulmonary embolism is present from what it is in the absence of embolism, particularly if a spasm of the remaining pulmonary vessels is produced by the embolus.

Induction of Puberal Changes in Young Women with Primary Amenorrhea

DRS. W. O. THOMPSON, S. G. TAYLOR III and PHEBE K. THOMPSON, Chicago: Observations have been made on the effect of various estrogenic materials in the treatment of young women who have not matured sexually and who present a syndrome corresponding to that observed in many eunuchoid males whose testes have not descended. In such women, large doses of estrogenic material produce (1) development of the secondary sexual characteristics of the female, including the growth of the external and internal genitalia, the development of the breasts, the growth of axillary and pubic hair and the onset of intermittent uterine bleeding resembling menstruation; (2) a moderate increase in body weight, most noticeable in the buttocks, thighs and hips, augmenting the feminine appearance; (3) an increase in muscular strength, bodily vigor and mental acumen and (4) an increase in sex consciousness with a corresponding change in emotional status.

DISCUSSION

DR. C. M. MACBRYDE, St. Louis: It is known that the use of large doses of estrogenic material in experimental animals leads to damage to the ovaries which may be more or less permanent. That thought should be kept in mind when we treat eunuchoid persons. Perhaps it would be wise to emphasize the point that an attempt should be made to see whether stimulating therapy is effective; perhaps we have all been too eager to give up the stimulating therapy too soon. Do the changes Dr. Thompson and his associates produced disappear after treatment is discontinued, and must patients with this condition be treated indefinitely with estrogenic material to maintain the results as shown?

DR. S. G. TAYLOR III, Chicago: During the administration of stilbestrol the nipples of one of these patients became black, and a dark line developed between the umbilicus and the lower part of the abdomen in the midline. The umbilicus became deep black. There has been a slight decrease in this pigmentation during the past month despite the continuation of treatment. I wonder if any one has an explanation.

DR. W. O. THOMPSON, Chicago: Damage to the ovaries as the result of administration of large doses of estrogenic material has been demonstrated, I think, and there is, of course, in the male damage to the testes as the result of administration of testis hormone, which may be so pronounced that spermatogenesis is abolished. The damage to the testes appears to be temporary, and recovery takes place when treatment is discontinued. All the patients I have shown received gonadotropic material which has been ineffective. There unfortunately is no gonadotropic material prepared from the pituitary gland itself that is of much clinical value. While we may have made an occasional woman menstruate during the administration of certain pituitary preparations, by and large all of them are of little value at the present time. The gonadotropic material from the serum of the pregnant mare is also a great disappointment. The most effective gonadotropic material available is that prepared from the urine of pregnant women, but its value in the female is still undetermined. It is not always easy to decide when hypogonadism is primary and when it is secondary. One of our eunuchoid men with both testes high in the inguinal canal has recently shown descent of both testes and genital growth with chorionic gonadotropin. The women reported in this study did not respond to the gonadotropic materials available now. While estrogens may theoretically damage the ovary, the changes produced were so striking that their use seems not only justifiable but desirable in women with primary amenorrhea. I should agree that it is a good therapeutic principle in hypogonadism to try the effect of stimulation therapy first and resort to substitution therapy if it fails.

DR. ELMER L. SEVRINGHAUS, Madison, Wis.: I think Dr. Thompson has made some statements that are too broad in his closing remarks. In his experience the serum from pregnant mares has been disappointing, but we have had distinctly good results with this type of thing. Dr. MacBryde reported another difficulty—that there is a time factor. We know that adolescence takes time and that an artificially produced adolescence takes time. If cases can be carried to the point of pregnancy and delivery I think it shows something can be done. Several of our cases have been successful in this sense.

DR. W. O. THOMPSON, Chicago: I am not entirely in agreement with Dr. Sevringhaus about the value of pituitary gonadotropin. It is of some interest that our third patient, who showed such striking development of secondary sexual characteristics during the administration of estrogenic material, had been treated by Dr. Sevringhaus for a year with a pituitary preparation without any effect.

The Peroral Use of Methyl Testosterone in Testicular Deficiency

DRS. E. PERRY MCCULLAGH and H. R. ROSSMILLER, Cleveland: The clinical effects of methyl testosterone following its oral administration are compared with those of testosterone propionate administered by injection. The study is based on 19 cases. The drug has been administered over periods varying from a few weeks to ten months. The patients treated include some with severe prepuberal hypogonadism, primary pituitary disease with secondary hypogonadism and functional impotence. The observations indicate that methyl testosterone given perorally has a strong androgenic activity in that it produces in persons with androgenic deficiency a definite increase in the size of the penis and prostate gland, a general increase in body hair and increase in sexual potency. There is a striking increase in energy and endurance and the development of the typical aggressiveness of the normal male. The doses used have varied from 25 to 300 mg. daily. A gain in body weight of approximately 10 to 20 pounds (4.5 to 9 Kg.) within three weeks of beginning the administration of the drug has been noted. This is shown to be associated with retention of sodium, chloride and nitrogen. Consistent elevations in the basal metabolic rate have been seen after relatively large doses. Such increases in basal metabolism have amounted to as much as 54 per cent. Basal metabolic rates as high as plus 38 per cent have not been associated with the clinical picture of hyperthyroidism. The rate of growth may be greatly aug-

mented by the use of methyl testosterone. In 1 instance we have seen the growth rate increase from levels of 1 inch (2.5 cm.) a year before the age of 19 to 5½ inches (14 cm.) a year over a ten month period during the use of the drug. Continued large doses may cause oligospermia, such as has been reported after the use of testosterone propionate. An interesting side effect has been the development of gynecomastia in several of the cases.

DISCUSSION

DR. M. A. BLANKENHORN, Cincinnati: Have the authors made a decision of what the total growth is going to be? Has the actual growth been increased or merely accelerated? Will there be a taller youth or will the youth have reached his height sooner in life?

DR. E. PERRY MCCULLAGH, Cleveland: The two questions refer virtually to the same thing. We have been interested in the problem for a long time, and in one of our previous publications we purported to show that large doses of testosterone propionate given to certain persons did apparently cause a more rapid epiphysial closure than had appeared previously and in 1 or 2 there was a more rapid than normal closure of the epiphyses. We do not know whether that will occur with this material or not. So far there is no evidence that it does, but it is a factor that must be considered seriously, because it may work just as do the hormones which are secreted in certain adrenal tumors, in which rapid growth is connected with rapid epiphysial closure. Under these conditions persons grow more rapidly than normal, but the rate of epiphysial closure not only exceeds normal but exceeds the growth rate as well, so that the individual affected is eventually shorter than normal. We have seen rapid growth of this type in 1 person, who is already 6 feet (182 cm.) tall. In such cases care should be taken not to continue growth unless the epiphyses can be closed at a rate which is parallel to the growth rate.

Effect of Extracts of Anterior Lobe of Pituitary Gland on Diabetes, Retarded Growth and Sexual Development

DRS. JAMES A. GREENE, L. E. JANUARY and L. W. SWANSON, Iowa City: The effect of administration of extracts of the anterior lobe of the pituitary gland has been observed in 3 patients with diabetes mellitus and dwarfism. The alterations produced in the calcium, phosphorus, nitrogen and sulfur metabolism, the growth rate, the sexual development and the diabetes were ascertained. The metabolic studies showed an immediate and a later effect of the extract. The growth rates increased and sexual development occurred. The diabetes was improved in the patient 26 years of age but was not altered in the two 17 and 18 years of age.

DISCUSSION

DR. HENRY T. RICKETTS, Chicago: What extract was used and what was the dose? And was the extract tested in animals to determine whether it has a diabetogenic factor in large doses? I think it is interesting that the extracts which seemed to be effective in producing growth apparently did not affect the diabetes. I am not sure that the effect of the extract on growth has been clearly established. Children who have controlled diabetes may grow without anything else having been done. The first patient presented was sent home from the hospital and was supposed to be on good control while at home. However, he returned to the hospital with an increase in insulin requirement, having stopped taking pituitary extract and also stopped growing. Does this mean that the pituitary extract had been effectively used, or does it simply mean that the patient was a little lax in his diet at home and when admitted to the hospital was again controlled with large doses of insulin and, as would be expected, resumed growth?

DR. W. O. THOMPSON, Chicago: What pituitary extract was used? We have tried to produce growth in man with pituitary extracts and so far we have not been able to find one that definitely accomplishes this end.

DR. JAMES A. GREENE, Iowa City: The extracts used were those marketed by Parke, Davis & Co. What made our first patient's diabetes get better, I do not know. It is true that his diabetes got worse at home and was probably due to laxity in the diet. We now have several patients with dwarfism who have grown; the oldest is a man aged 26 whom we have followed for four years. He has grown 3¾ inches (9.5 cm.), the epiphyses have closed, and he looks like a man now. One factor which has to be taken into consideration is that we have to give these extracts time to work.

Secretin in Determining Pancreatic Function

DR. H. M. POLLARD and LILA MILLER, PH.D., Ann Arbor, Mich.: By the use of secretin, pancreatic-duodenal juices have been secured and analyzed with respect to concentration of amylase, trypsin, bicarbonate, bile pigments and hydrogen ion concentration. Thirty-one persons were used as subjects to furnish data for the pancreatic response. They included a control group of 8 normal persons and in addition 5 patients with severe diabetes, 7 with carcinoma of the pancreas, 7 with pronounced cholecystic disease, 2 with stone of the common bile duct, and 2 with chronic pancreatitis. On the basis of these data, the value of this test as a diagnostic aid was considered.

DISCUSSION

DR. HENRY T. RICKETTS, Chicago: A patient recently studied had severe general calcification of the pancreas with complete pancreatic achylia yet with his diabetes controlled by as little as 10 units of insulin. Therefore a disturbance of the external pancreatic function does not necessarily imply great severity of the diabetes itself.

DR. CLARENCE BERNSTEIN, Chicago: If there is a carcinoma in the body of the pancreas the external secretion may be disturbed, but in the cases of carcinoma of the head of the pancreas presented the figures show that there was much bile in all specimens of duodenal contents. Were these cases of completely obstructive jaundice and did they show jaundice clinically?

DR. WALTMAN WALTERS, Rochester, Minn.: Most of the obstructions caused by cancer of the head of the pancreas are not true anatomic obstructions but are functional. One can demonstrate that the lumen of the pancreatic portion of the common bile duct has been squeezed but not completely occluded by the tumor in the head of the pancreas. This squeezing is occasionally due to inflammation associated with the carcinoma. At the present time, in the management of lesions of the biliary tract errors sometimes occur in determining the presence or absence of associated chronic pancreatitis. The surgeon is dependent on the feeling of the pancreas to determine whether chronic pancreatitis is present. Postoperatively there is an opportunity to check the diagnosis by cholangiographic studies. If pancreatitis persists, its squeezing effect on the pancreatic portion of the common bile duct is apparent not only by the narrowing of its lumen and a persisting increase in the midportion of the duct but by delay in the emptying time of the duct as well. Improved tests of pancreatic function have been of considerable assistance in determining the presence of pancreatic disease. This has been true not only as far as the study of external pancreatic secretion itself following the intravenous injection of secretin, as originated by Lagerlöf, is concerned but also in the study of values for the activity of amylase and lipase in the serum, as Comfort and Osterberg have shown. These observers have found the values for amylase and lipase to be almost constantly elevated if determined within a few days after the onset of acute pancreatitis. The values for amylase usually return to normal within three or four days, whereas those for lipase may be elevated for as long as ten to fourteen days or longer after onset of the attack. Comfort and Osterberg have shown also that increased concentration of lipase in the serum in cases of obstructive jaundice denotes that the pancreas is involved in the process; if the clinical data point to malignant obstruction, the elevation of values for serum lipase localizes the malignant condition in the pancreas rather than in the biliary tract, for these authors have shown that normal values for serum lipase obtain almost universally in malignant lesions of the biliary tract.

DR. H. M. POLLARD, Ann Arbor, Mich.: The test requires much more study and analysis, especially on normal persons, before we shall be able to evaluate abnormal readings. In doing these thirty-one tests throughout last year, we utilized a full time chemist for the analyses, and, in addition, Dr. Miller and I

devoted considerable time to the details of obtaining the samples and assisting in the analysis. Consequently at the present time I do not consider that the test is a simple one, but I am convinced that it offers valuable information. In answer to Dr. Bernstein, the patients who had carcinoma of the head of the pancreas with obstruction did show clinical jaundice. The cost of the material is still high, and I do not know of any other source than the one pharmaceutic house in Sweden. The suggestion of repeating the test after removal of the obstruction to the pancreatic duct is an excellent one. We have not done this but it would add positive information. The use of this test in evaluating the presence or absence of pancreatitis offers good theoretic possibilities, and we have been able to apply it in 2 cases with confirmatory results. I believe that the test has a definite value in evaluating associated pancreatic disease in the presence of severe disease of the gallbladder.

A Study of Gold Metabolism and the Fate of Gold Injected in the Treatment of Arthritis

DR. R. H. FREYBERG, W. D. BLOCK, PH.D., and O. H. BUCHANAN, M.S., Ann Arbor, Mich.: While patients with rheumatoid arthritis were receiving increasing amounts of either myochrysine, gold sodium thiosulfate or aurolsulfide at weekly intervals (for approximately six weeks), the concentration of gold in the blood and the urinary excretion of gold were measured daily by a new, highly sensitive, photoelectric colorimetric method. In addition, on the day of administration of the gold salt the content of gold in the blood and urine was determined one, two, four, six and twenty-four hours after injection. After the weekly dose of medicine became standardized similar determinations of gold were made at approximately monthly intervals throughout the period of treatment and for several months thereafter. Occasionally the concentrations of gold in synovial fluid and blood were measured simultaneously. In many other patients occasional determinations of gold in blood and urine were made during and after periods of chrysotherapy.

As the amount of gold salts administered was increased in the manner commonly employed, the blood concentration and urinary excretion of gold increased slightly but the elimination was much slower than the rate of administration, so that gold remained in the body in significant amounts often for months after its administration ceased.

DISCUSSION

DR. WALTER L. PALMER, Chicago: This last year we looked up the literature on gold therapy to see if there is any valid evidence that this new cure is better than any other new cure for arthritis. We were not able to convince ourselves that there is any real advantage in gold therapy over any other therapy, including psychotherapy. There is good evidence that gold therapy is dangerous and so, until we can prove that it has some value, it seems to me that the medical profession should not use it as generally as it is now being used. There came to our attention last spring a woman aged 47 who, because of mild arthritic symptoms, had been given by her physician four injections at weekly intervals of gold thiosulfate, 50 mg. a dose, receiving a total dose of 200 mg. She had no symptoms of toxicity until after the last injection. Six days after this last injection she suffered nausea and vomiting and diarrhea. These symptoms persisted for ten days. The patient was brought to the hospital in a stage of acute dehydration with profound diarrhea and died six days later. The autopsy showed extensive ulcerative gastroenteritis, particularly involving the ileum; the mucosa was entirely gone. Chemical studies disclosed the presence of gold in all tissues studied, particularly in the liver and spleen and intestine. The death occurred about three weeks after the last injection of gold, and all the symptoms occurred after the last injection.

DR. CARL V. MOORE, St. Louis: I was much interested in the appearance and increase of gold in plasma. Do the authors know in what form this gold is present? Is it hooked up, for instance, with the serum globulin?

DR. CLARENCE BERNSTEIN, Chicago: Could gold sulfide be recovered in the stool, and, if so, would this be a better indication that it had not been absorbed?

DR. CHARLES A. DOAN, Columbus, Ohio: What proportion of patients who tolerated this treatment seemed to be clinically improved? Has any type of allergic reaction been noted early in the course of gold therapy in those patients who did not tolerate it so well?

DR. CECIL STRIKER, Cincinnati: What is the time relationship between the injection of gold and the appearance of gold in the synovial fluid, and how long after injection is discontinued does the gold persist in the synovial fluid?

DR. R. H. FREYBERG, Ann Arbor, Mich.: Our paper is entitled "A Study of Gold Metabolism" and we did not plan to discuss the problem of clinical value. We prefaced this discussion with the statement that we had observed definite benefit which we thought was due to the use of gold salts, but we also observed reactions which were serious in some cases. We observed our patients carefully for a long time before gold therapy was used. We have seen many patients who, when given gold, had definite clinical benefit that persisted for as long as we have followed them, so we feel that gold therapy has value in some patients. I should like to know whether Dr. Palmer has observed many patients treated with gold when he questions its value. I questioned its value before I used it. In some patients there is no benefit. We do not recommend the use of gold salts by general practitioners as the treatment exists at present. Before we use gold salts we explain the situation and let the patient decide whether or not he wishes this form of treatment; we give an honest evaluation of the possibility of good and harm, and if he wants it used we employ it. We are extremely careful in its use and make frequent examinations of the blood and urine for any indication of intolerance. I am sure that if great caution is used intolerance will often be recognized and many serious reactions avoided. The length of time the drug is used, the dose and the route of administration are important with regard to reactions. We believe that intravenous administration is not the preferable route. We have not observed any benefit before six or eight weeks after treatment is begun; consequently we see no justification for the intravenous use of a drug which acts so slowly if it can be successfully administered by another route. On the basis of the results of our metabolic studies and because we have encountered more reactions with large doses of the drug, we are at present using doses smaller than are commonly employed. I am sure this is safer. In answer to Dr. Moore's question, we have not determined the form in which gold exists in the blood. We have separated the corpuscles from the plasma and then have found gold only in the plasma. We have to date used colloidal gold sulfide only by intramuscular and oral administration. Dr. Bernstein asked whether analyses have been done on feces. We are doing that now in our study of patients and have studied this in animals. We have found some gold in the feces of animals given gold salts intramuscularly, but whether after colloidal gold sulfide has been given orally there are significant amounts of gold in human feces needs to be determined. We have observed some patients soon after the drug has been given intravenously who show a relatively small amount of gold in the blood. Our studies on animals have shown that the reticuloendothelial cells of the liver and spleen take up gold when it is given as colloidal aurol-sulfide, intramuscularly. We cannot answer Dr. Doan's question about the incidence of toxic reactions. We do not see a large number of patients. About 1 in 4 patients we treat with gold salts will not be able to tolerate the drug, but often we stop treatment on extremely slight evidence of intolerance. We estimate that about 75 per cent of the patients who have been able to tolerate the drug and who have continued treatment have been benefited by it.

Prevention of Peritonitis

DRS. J. A. BARGEN, W. J. TENNISON and C. F. DIXON, Rochester, Minn.: This is an analysis of the effect of antiperitonitis vaccine in 3,000 patients who had surgical procedures performed on the large intestine. A mixture of the green-producing streptococci and Escherichia coli have been used in a vaccine against peritonitis in patients who were to have intestinal operations since October 1928. The early impressions from the use of this vaccine as part of a preoperative program were favorable. In recent years a well controlled experiment has been

conducted in which every alternate patient who anticipated an intestinal operation received the vaccine.

DISCUSSION

DR. JOHN G. MATEER, Detroit: To what degree has the dose of the vaccine been reduced in order to avoid the more severe febrile reactions and the resulting higher mortality from subsequent peritonitis of patients having reactions of this type?

DR. GEORGE E. WAKERLIN, Chicago: Was there any preliminary experimental work on animals?

DR. J. A. BARGEN, Rochester, Minn.: Animal experiments were performed by Dr. Siegfried F. Herrmann at the Institute of Experimental Medicine under the direction of Dr. Mann. Extensive experiments were performed in which dogs were inoculated with fecal streptococci and Esch. coli intraperitoneally. After the injection of such a bacterin extensive intestinal operations were performed on the dogs. The incidence of fatal peritonitis in dogs so treated was low, whereas the incidence of peritonitis in a similar series of dogs which did not have the vaccine preoperatively was high. It was these striking results which led us to administer a similar vaccine to human beings before performing major intestinal operations. Reduction in fatal peritonitis in patients who have had such a bacterin has been striking. The problem has been studied from many different angles. There is a reduction in the total number of patients who have succumbed to peritonitis, there is a greatly reduced incidence of peritonitis when one considers the problem by operation, and there is a decided reduction in mortality when one considers the problem by surgeons who have operated. In reply to Dr. Mateer's question about the dose, I would say that a total of 1 cc. of a mixture consisting of equal parts of streptococci and Esch. coli suspended in 10 cc. of physiologic solution of sodium chloride is given intraperitoneally. Such a mixture will contain about 500 million of the killed streptococci and 500 million colon bacilli.

Circulating Blood Volume in Human Subjects Exposed to Hot Environments

DR. FORD K. HICK, NATHANIEL GLICKMAN, M.S., and DRS. M. M. MONTGOMERY and ROBERT W. KEETON, Chicago: Healthy medical students were the subjects of experiments. Under basal conditions an initial determination of the blood volume was carried out by the dye injection procedure (T1824) while the conditions were comfortable for the nude subject. On its completion the temperature was increased so that regulation of evaporative heat was dominant and after an appropriate length of exposure (one hundred to two hundred and fifty minutes) the determination of the blood volume was repeated.

After fairly short (one hundred minutes) exposure to a temperature of about 98 F. an increase in the volume of circulating blood has been observed amounting to 11 per cent, despite considerable loss of water from the body by evaporation. In a longer exposure to extremely hot conditions (112 F. for two hundred and twenty minutes), a fall of as much as 7 per cent in blood volume has been observed. After free sweating in hot conditions certain subjects showed no change in blood volume even after losing as much as 900 Gm. of water in sweating.

Changes in blood protein reflect the concentration and dilution of plasma implied. Leukocytes or red cell counts do not accurately indicate these adjustments.

Certain subjects, presumably more facile in their regulation of heat, can withdraw water for sweating from stores within the body without affecting the circulating body fluids.

DISCUSSION

DR. ROBERT W. KEETON, Chicago: Estimations of the plasma volumes from day to day do not always show the same values. The exposure of the body to warm environments causes a peripheral vascular dilatation and a transfer of blood from the interior of the body to the exterior. This is mirrored by the reduction of the blood in the lungs, as shown by the increase in the vital capacity. When a subject stands on his feet there is a decrease in the circulatory volume of blood, which returns to its original value after thirty to sixty minutes. All these facts indicate that there is a rather ready exchange between the volume of active circulating blood and the volume of reserve blood. The requisitioning of new supplies of blood from this source is one of the first adjustments of the circulation to increased temperatures. This in turn leads to the conclusion that the blood volume is undergoing all the time phasic adjustments, and its value at any one time is dependent on the physiologic state of the person at the moment.

DR. GEORGE E. WAKERLIN, Chicago: Has Dr. Hick determined with what rapidity these changes occur in the normal human being?

DR. FORD K. HICK, Chicago: These changes take place in the human being rather rapidly within forty minutes or sooner. With regard to animal experiments on heat regulation, I do not believe there is any possibility of transmitting any data from animal to human physiology in such an experiment because of the difference in heat-regulating mechanisms.

The Clinical Value of Sleeping in the "Head Up" Position

DRS. A. R. MACLEAN and E. V. ALLEN, Rochester, Minn.: Man is one of the few animals which lead a life in two planes, the vertical during activity and the horizontal during sleep. As a result of this postural change, he is susceptible to ailments which have postural components. We have studied two such disorders, orthostatic hypotension and orthostatic tachycardia. Our studies indicate that therapeutic methods which diminish the range of postural change have a place in the treatment of these disorders.

In primary orthostatic hypotension, as well as in secondary orthostatic hypotension after extensive sympathectomy for essential hypertension, the use of the "head up" bed has resulted in great improvement in the arterial blood pressure in the erect posture. The symptoms of syncope and weakness in the erect posture have dramatically disappeared, and patients are capable of existing in the upright position during the day. However, sleep in a horizontal bed perpetuates the inability to stand erect or completely destroys the advantages gained by sleeping in the head up position.

Some patients with orthostatic tachycardia, a syndrome which in many instances is comparable to those designated as "effort syndrome," "irritable heart" or "neurocirculatory asthenia," have been relieved of their symptoms by sleeping in the head up position. Likewise some patients with hypertensive headaches which occur only at night have been benefited. Other conditions have been studied. The physiologic adjustments which follow this type of treatment are complex, but some of them are fairly well understood.

DISCUSSION

DR. JOHN W. SCOTT, Lexington, Ky.: Certain it is that since the days of early English physiologists we have always thought that man compensated for the upright position by splanchnic control, and yet, as I understand the paper, the authors assume that this has little or nothing to do with the relief of these patients but rather they ascribe it to a better return of venous blood. It seems to me difficult to understand why perhaps we all should not sleep upright. Would we be better off? We pay the price for the assumption of the upright position and I find great difficulty in explaining these interesting results the way the authors have done.

DR. E. V. ALLEN, Rochester, Minn.: This simple procedure will not benefit simple morning exhaustion without a postural component defined as orthostatic decrease in blood pressure. Moreover, in our experience it has not benefited 3 patients who have had epilepsy which occurred chiefly at night. It has benefited several patients who have headache on awakening or who are awakened by headache. It is important to remember that since patients who complain of morning exhaustion improve during the day subjectively and objectively the study of blood pressure and pulse rate must be carried out in the morning, for objective evidence which accounts for symptoms may be absent or minimal in the afternoon.

DR. J. DEWEY BISGARD, Omaha: Often normal surgical patients, when first getting out of bed after an operation, complain of dizziness and may collapse with a big fall in blood pressure as do patients with postural hypotension. Those patients kept in Fowler's postion after operation have fewer of these symptoms than do those kept flat in bed.

Dr. A. R. McLean, Rochester, Minn.: Our conception of orthostatic hypotension has changed significantly. We previously thought that the hypotension represented a disturbance of the sympathetic nervous system. We now feel that the drop in blood pressure is merely a secondary phenomenon resulting from diminished return of venous blood. This defect in return of venous blood can be demonstrated by the Flack test. The evidence of a disturbance in the autonomic nervous system had been the lack of a cardiac accelerating mechanism, a deficiency in sweating and the drop in blood pressure on standing. In our cases of orthostatic hypotension we have been able to demonstrate normal arteriolar reflex vasoconstriction and vasodilatation as a result of changes in environmental temperature. In 1 case, in which remarkable improvement occurred from the use of a head up bed, we have been able to demonstrate the reestablishment of normal sweating. It appears to us that in cases of orthostatic tachycardia orthostatic hypotension would develop if the cardiac accelerating mechanism failed.

Rate of Diodrast Excretion During Intravenous Urography as a Test of Renal Function

Drs. Joseph C. Edwards, Thomas Findley and H. L. White, St. Louis: The large amount of diodrast required intravenously for roentgen visualization of the renal pelvis imposes a far heavier load on the function of tubules than do the amounts of phenol red and other dyes in common use. The iodine method of White and Rolf has been made suitable for routine office use, and the amount of diodrast excreted during the thirty minutes following injection has been compared with simultaneous urea clearance. Normal adults excrete about 40 per cent of the injected iodine under the conditions usually employed in pyelography. The effects of dehydration, fasting and pitressin have been examined, and normal value has been established in adults for the usual quantities of both diodrast and diodrast compound. The test measures neither the flow of renal plasma nor the Tm (maximal tubular excretion) value of Smith but appears to be a valuable addition to urologic technic because it is fully as sensitive as urea clearance, requires no complicated analytic procedure and imposes no additional expense or inconvenience to the patient undergoing roentgen study.

A group of twenty-eight City Hospital interns and Washington University Medical School students were studied as a normal group. All had normal urea clearances, blood pressures, blood urea nitrogen levels and urine.

A group of 12 patients with various degrees of essential hypertension, chronic glomerular nephritis and cardiac decompensation were studied. Urea clearances were performed simultaneously in 2 normal and 3 abnormal patients. Diodrast inulin clearances were also done and were well correlated with the diodrast iodine excretions in the thirty minute period. The blood iodine is at maximal tubular excretion for the first fifteen or twenty minutes of the test.

The abnormal group excreted about 30 per cent of 2.3 Gm. of iodine injected as 20 cc. of diodrast in thirty minutes, while the normal was 40 per cent. The worse the renal function, the less iodine there was excreted. There was comparatively little difference among tests done before breakfast (during fasting) and those done after the subjects had food.

The effect of pitressin decreased the urea clearance without appreciably affecting the excretion of diodrast.

Excretion of Porphyrin in the Urine in Alcoholic Cirrhosis and After Episodes of Hepatic Coma

Dr. Samuel Nesbitt, Rochester, Minn.: During a qualitative and quantitative study of the excretion of ether-soluble porphyrin in the urine of patients suffering from a variety of hepatic diseases, 4 instances of severe alcoholic cirrhosis of the liver were encountered. The persons concerned were observed for extended periods during which they exhibited repeated transient episodes of neurologic manifestations ranging from confusion and mild psychotic states, sometimes with pathologic neurologic signs, to deep hepatic coma. By means of daily quantitative determinations it was ascertained that these patients excreted abnormally large amounts of coproporphyrin in their urine and that this value was diminished before and during periods of acute hepatic insufficiency, only to be abruptly increased as the patient emerged from the acute episode. The porphyrin has been isolated and identified as coproporphyrin I and III.

DISCUSSION

Dr. C. J. Watson, Minneapolis: I agree that the variation in the excretion of porphyrin in these cases represents a variation in clearance. These patients have profound hepatic damage with suppression of renal function. We have seen a similar example in a patient with acute porphyria excreting large amounts of the zinc complex of uroporphyrin. This patient was admitted to the hospital with severe abdominal colic, severe vomiting and moderate dehydration. During the first twenty-four hours the urinary output was 160 cc.; this increased rapidly, probably as a result of the parenteral administration of fluids and dextrose. With this there was an increase in the output of the zinc complex from 10 mg. during the initial phase to 90 mg. when the fluids had increased. In the past it has been customary to determine simply the total excretion of coproporphyrin in the urine. Our information so far has concerned only the values for the total of the two isomers. In the future increased importance will undoubtedly become attached to the ratio between isomer types I and III in the urine and feces since it is certain that coproporphyrin I has significance entirely different from that of the type III isomer. The synthesis of the type I isomer is independent of hemoglobin synthesis, although the available evidence indicates that the formation of type I is related in some way to the rate of erythropoiesis in the bone marrow. Therefore it is not surprising that patients with cirrhosis who have a red bone marrow and not infrequently have at least a mild increase in the rate of destruction of the blood should exhibit increased formation and excretion of the type I isomer. Also, because of the hepatic damage, there is a shunt of the coproporphyrin I into the urine so that with cirrhosis of the liver we commonly encounter increased type I in the urine. This is comparable to urobilinogen excretion in similar cases. Patients with macrocytic anemia with excessive amounts of urobilinogen in the feces and large amounts in the urine have an oversupply of the substance with inability of the liver to handle the amounts returned to it. The question of significance of the type III isomer is more difficult of interpretation. On theoretic grounds the formation of this isomer could be regarded as related to the formation or destruction of hemoglobin. There is no evidence that coproporphyrin III is formed during the simple destruction of hemoglobin, but there is much evidence that it is formed when there is a disturbance of the formation of hemoglobin in the bone marrow, as in lead poisoning or other types of poisoning. It is of interest that some patients with cirrhosis have been noted to have a predominance of type III in the urine. Most patients, it is true, excrete chiefly the type I isomer. The fact that excretion of type III has been noted in some and that this is most often associated with some form of poisoning may provide a means in the future of obtaining more information about the etiology of hepatic cirrhosis.

Dr. Hugh R. Butt, Rochester, Minn.: Were vitamin supplements given and, if so, was there any apparent effect on the excretion of porphyrin?

Dr. Samuel Nesbitt, Rochester, Minn.: It is interesting that these patients did recover from such acute episodes, and this may be attributed to the intensive vitamin therapy, since that was the one innovation in their medical care. The routine management always included vitamin supplements, and at the first appearance of what might suggest the onset of such an acute episode of hepatic insufficiency intensive vitamin therapy was instituted which included the daily intravenous administration of at least 100 mg. of nicotinic acid, 100 mg. of thiamine hydrochloride, 100 mg. of ascorbic acid and 1 to 2 mg. of a vitamin K preparation. We were never able to demonstrate to our satisfaction that any one of these vitamins or any combination of them produced any decrease in the excretion of porphyrin in the urine of many patients having various diseases of the liver. When the particular patients were receiving the most intensive vitamin therapy and after they had responded to treatment, the excretion of porphyrin in the urine was abruptly increased.

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

18:257-292 (Feb.) 1941

Treatment of Acute Intestinal Obstruction. F. K. Boland, Atlanta, Ga.—p. 257.
Urinary Lithiasis. J. U. Reaves, Mobile.—p. 261.
Syphilis: Control Program in a Mining Community. R. L. Stewart, Acmar.—p. 265.
Diagnosis and Treatment of Coronary Occlusion. J. C. Gladney, Jasper.—p. 267.
Discussion of Hydatidiform Mole. T. M. Boulware, Birmingham.—p. 269.
Role of Allergy in Pediatric Practice. A. C. Gipson, Gadsden.—p. 272.
Carbuncle of Face, Septicemia and Pulmonary Abscess: Recovery Following Sodium Sulfathiazole Intravenously: Case Report. T. F. Scofield, Birmingham.—p. 274.

American Heart Journal, St. Louis

21:133-256 (Feb.) 1941

Preliminary Investigation of Therapeutic Value of Lanatoside C (Digilanid C). G. Fahr and J. LaDue, Minneapolis.—p. 133.
Calibrated Phonocardiography: New Technic for Clinical Use. E. Mannheimer, Stockholm, Sweden.—p. 151.
*Hemoptysis in Rheumatic Heart Disease. L. Wolff and H. B. Levine, Boston.—p. 163.
Form of Volume Pulse in Finger Pad in Health, Arteriosclerosis and Hypertension. J. B. Dillon and A. B. Hertzman, St. Louis.—p. 172.
Spontaneous Volume Changes in Extremities. D. I. Abramson and K. H. Katzenstein, with assistance of Fanny A. Senior, Cincinnati.—p. 191.
Effects of Nitrites and Xanthines on Coronary Inflow and Blood Pressure in Anesthetized Dogs. N. H. Boyer and H. D. Green, Cleveland.—p. 199.
Relationships of Lead I, Chest Leads from C_5, C_4 and C_3 Positions and Certain Leads Made from Each Shoulder Region: Bearing of These Observations on Einthoven Equilateral Triangle Hypothesis and on Formation of Lead I. C. C. Wolferth, Mary Miller Livezey and F. C. Wood, Philadelphia.—p. 215.
Use of Cathode Ray for Recording Heart Sounds and Vibrations: III. Total Cardiac Vibrations in 100 Normal Subjects. J. R. Smith, J. C. Edwards and W. B. Kountz, St. Louis.—p. 228.

Hemoptysis in Rheumatic Heart Disease.—Wolff and Levine state that among the 521 patients with rheumatic heart disease admitted to the Beth Israel Hospital between 1928 and 1937 inclusive 50 had hemoptysis prior to admission or during hospitalization. The symptoms associated with the hemoptysis varied; some patients had none, others complained of pain in the chest, palpitation, dyspnea, cyanosis, wheezing, acute pulmonary edema, weakness, faintness and collapse. The three most common symptoms were palpitation, pain in the chest and dyspnea. The average age of the patients was 33.4 years; the youngest patient was 14 and the oldest was 54. Mitral stenosis was present in every case (except one, in which the hemorrhage was caused by a lung abscess), pulmonary infarction was diagnosed in 23 and, prior to the onset of hemoptysis, congestive failure was present in only 8 cases. The hemorrhage was accounted for by pulmonary infarction in almost half of the patients. Pulmonary infarction was found in 7 of the 8 cases of congestive failure and in only 2 of the 9 cases in which the size of the heart was normal. Following the initial hemoptysis the size of the heart increased progressively over a period of many months and, at postmortem examination of one of them, pulmonary arteriosclerosis and multiple thrombosis were found. Pulmonary infarction is the most likely cause of hemoptysis in the presence of congestive failure, but if the patient has no cardiac enlargement it can be excluded. If pulmonary infarction is present in the absence of cardiac enlargement, and particularly if hemoptysis is followed by a progressive increase in the size of the heart, pulmonary arteriosclerosis may be the underlying cause. In most of the remaining cases the hemoptysis was caused by mitral stenosis alone, without gross evidence of congestive failure. Hemorrhage may be caused by active rheumatic infection. There was such evidence in 12 cases. When hemoptysis occurs in a case of rheumatic heart disease and intercurrent pulmonary disease and left ventricular failure can be excluded, it may be assumed that mitral stenosis is present. Hemoptysis in such cases may help to distinguish between an Austin-Flint and an aortic regurgitation murmur, or in the diagnosis of mitral stenosis. At the time at which this study was completed, the authors point out that 33, or 66 per cent, of the 50 patients are dead; the average survival following the initial hemoptysis was thirty-two and a half months, varying from one day to more than five years. The average interval from the initial hemoptysis to the last follow-up examination of the 17 patients who are still living has been thirty-nine months and, to date, only 5 of these have survived five years or longer. Half of the patients with slight cardiac enlargement died within one or two days after hemoptysis, and two thirds died within a year. As these deaths were of patients in whom the prognosis was usually excellent, it is obvious that hemoptysis in such cases is a grave prognostic indication. Among the remaining patients the mortality was higher and the survival shorter than would have been expected of patients with cardiac enlargement and congestive failure alone. The mortality was higher among the patients with pulmonary infarction than in the series as a whole. Hemoptysis during pregnancy is not necessarily indicative of a bad prognosis, for the 2 pregnant women in the series survived the longest.

American Journal of Surgery, New York

51:309-552 (Feb.) 1941

Manchester Operation, with Special Reference to Its Development and Principles Involved in Its Technic. I. F. Frost, New York.—p. 311.
Acute Surgical Complications of Fractures. H. L. Albright, Boston.—p. 320.
Natural Adrenal Cortex Extract and Coagulation of Blood. F. R. Reed, Three Rivers, Mich.—p. 330.
Treatment of Persistent Occipitoposterior Position by 180 Degree Manual Rotation of Occiput. S. S. Rosenfeld, New York.—p. 340.
Ununited Fractures of Clavicle. R. K. Ghormley, J. R. Black and J. H. Cherry, Rochester, Minn.—p. 343.
Preparation of Autogenous Bone Grafts with Osteotomes. W. G. Stuck, San Antonio, Texas.—p. 350.
Use of Implantation Grafts in Healing of Infected Ulcers. K. M. Marcks, Allentown, Pa.—p. 354.
Surgical Removal of Hemangioma of Face. M. I. Berson, New York.—p. 362.
Study of Role of Amino Acids in Clot Retraction: Effect of Methionine in Restoring Normal Clot Retraction and Control of Bleeding in Essential Thrombocytopenic Purpura. H. M. Rabinowitz, Brooklyn.—p. 366.
Review of Malignant Melanoma of Mouth: Report of Case. H. Baxter, Montreal.—p. 379.
Spontaneous Internal Biliary Fistula. E. L. Eliason and L. W. Stevens, Philadelphia.—p. 387.
Staphylococcic Prostatitis Treated with Staphylococcus Toxoid. A. C. Drummond, New York.—p. 393.
*Healing of Tuberculous Nephrectomy Sinuses. M. E. Greenberger and I. Helfert, New York.—p. 396.
The Ideal Dressing for Clean Wounds. O. Tenopyr and F. M. Al Akyl, Brooklyn.—p. 399.

Healing of Tuberculous Nephrectomy Sinuses.—Greenberger and Helfert have used ozonized olive oil in the treatment of nonhealing incisions and sinuses following excision of a tuberculous kidney. They found that the oil stimulated healing and at the same time added to rather than detracted from the comfort of the patient. The technic consists of the daily instillation of a sufficient quantity of the ozonized olive oil to fill the sinuses completely. Since this preparation contains heat, moisture, labile ozonides of triolein and other unsaturated hydrocarbons, significant quantities of nascent oxygen are released into the tissues of the sinus walls, where it acts as a bactericidal agent and a stimulant to local cellular metabolism. Thus sterilization of the wound and proliferation of tissue are promoted without destroying surrounding healthy tissue. Under this therapy the wounds have in most cases healed at a constant and satisfactory rate. The exposed surfaces of gaping lesions assumed a clean and fresh aspect without excessive granulation or sloughing. Of the 15 cases in which solution of triolein ozonide in olive oil was used the sinuses in 13 have healed completely in from two to five months. One wound which showed no evidence of healing during two months with other types of therapy healed readily under this treatment to such an extent that revision was easily done. In the fifteenth patient the wound was healing satisfactorily and only a single small sinus remained when the patient left the hospital without consent.

Archives of Internal Medicine, Chicago

67:241-472 (Feb.) 1941

*Cardiac Lesions Associated with Chronic Infectious Arthritis. A. H. Baggenstoss and E. F. Rosenberg, Rochester, Minn.—p. 241.

Familial Nonhemolytic Jaundice: Constitutional Hepatic Dysfunction with Indirect van den Bergh Reaction. W. Dameshek and K. Singer, Boston.—p. 259.

Pneumococcic Pneumonia: Analysis of Records of 1,469 Patients Treated in the Los Angeles County Hospital from 1934 to 1938 Inclusive: III. Type-Specific Antipneumococcus Serum Therapy: Quantitative Relations Between Dosage and Results. F. J. Moore, R. E. Thomas, B. O. Raulston, A. Hoyt and J. D. Walters, Los Angeles.—p. 286.

*Studies on Old Age Pneumonia: II. Prophylactic Effect of Pneumococcus Polysaccharide Against Pneumonia. P. Kaufman, with technical assistance of A. Kacfely, C. O'Brien, C. Burnstein, S. K. Kling and W. Dmitruk, New York.—p. 304.

Further Studies on Human Cardiac and Voluntary Muscle: Possible Implications of Changes in Creatine, Phosphorus and Potassium Content, with Special Reference to Heart Disease. G. H. Mangun, Charleston, S. C.; H. S. Reichle and V. C. Myers, Cleveland.—p. 320.

*Hemochromatosis: Report of Case. A. Cantarow and C. J. Bucher, Philadelphia.—p. 333.

Estimation of Renal Function with Aid of Iodosecretory Index and New Ureosecretory Index: Improved Application of Creatinine Method for Determining Diuresis. J. T. Peters, New York.—p. 345.

Experimental Study of Reciprocating Rhythm. D. Scherf, New York.—p. 372.

Relation of Liver Function to Cirrhosis of Liver and to Alcoholism: Comparison of Results of Liver Function Tests with Degree of Organic Change in Cirrhosis of Liver, and with Results of Such Tests in Persons with Alcoholism Without Cirrhosis of Liver. H. B. Cates, Los Angeles.—p. 383.

Fatal Bronchial Asthma: Report of Seven Cases. B. Craige Jr., New Haven, Conn.—p. 399.

Diseases of Nutrition: Review of Certain Recent Contributions. H. R. Butt and W. V. Leary, Rochester, Minn.—p. 411.

Cardiac Lesions Associated with Chronic Infectious Arthritis.—At necropsy in 25 cases of chronic infectious (rheumatoid) arthritis Baggenstoss and Rosenberg demonstrated cardiac lesions in 20. Lesions identical with those of rheumatic fever were observed in 14 (56 per cent). Nonrheumatic cardiac lesions were present in 6 (24 per cent). In 10 of the 14 cases in which there were rheumatic lesions there was microscopic evidence that the inflammatory process was still active and progressive when death occurred. In 7 of these 14 instances the heart disease was judged to be an important factor in causing death. Also in only 7 of these 14 patients had signs or symptoms of heart disease been present during life. The high incidence of rheumatic cardiac lesions suggests a relationship between chronic infectious (rheumatoid) arthritis and rheumatic fever.

Old Age Pneumonia and Effect of Pneumococcus Polysaccharide.—Kaufman reports the work done with active immunization against pneumonia of inmates (more than 50 years of age) of the New York City Home with a capsular antigenic polysaccharide containing specific substance for type I and II pneumonia. During the winter of 1937-1938, 1,000 persons were immunized with 0.5 cc. of the polysaccharide containing 1 mg. of each active substance, and 1,120 persons were kept as controls. In 1938-1939 the same method was used except that 500 new patients were divided in such a way that every other one was inoculated with 0.5 cc. and alternates were kept as controls. Another thousand were taken from the old inmates and 500 were inoculated with 1 cc. containing *2* mg. of each active substance and 500 who had served as controls the previous year were again used as controls. In the first year there were 14 cases of pneumonia with 8 deaths among the 1,000 immunized persons. Among the 1,120 nonimmunized there were 63 cases of pneumonia with 47 deaths. The second year there were 9 cases of pneumonia with 5 deaths among the 750 immunized persons and 41 with 20 deaths among the 750 nonimmunized. When the second year's study is subdivided it is found that there were 4 cases of pneumonia with *2* deaths among the 250 inmates receiving 0.5 cc. of polysaccharide with 1 mg. of each active substance and 5 cases with 3 deaths among the 500 given 1 cc. containing *2* mg. of each active substance. In the smaller control group there were 15 cases of pneumonia with 8 deaths and in the larger control group *26* cases with 12 deaths. Among the total 1,750 inoculated persons there were 23 cases of pneumonia with 13 deaths, making the morbidity rate 13.13 and the mortality rate 7.4 per thousand. Among the total 1,870 controls the figures are 104 cases with 67 deaths and the respective per thousand figures 55.66 and 35.8. The course of pneumonia in the immunized group (length of disease and frequency of complications) was apparently not influenced by the inoculations. The prophylactic value seemed more pronounced in the first three quarters than in the last quarter of the year after immunization. The data show that the incidence and mortality rates of pneumonia were reduced not only for the types from which the active substances were isolated but also for other types. Further observation is necessary to corroborate the data. A group like the one used is particularly suited for immunizations against pneumonia, as among such a population the high incidence, mortality and case fatality rates and the frequency of repeated attacks make active immunization a practical problem. As postoperative pneumonia is a dreaded complication in this age group, immunization with polysaccharide may considerably reduce its incidence.

Hemochromatosis.—Cantarow and Bucher report a case of hemochromatosis because of the following atypical factors: 1. Glycosuria was absent and the dextrose tolerance was significantly decreased in spite of the unusual quantity of iron in the liver and pancreas. *2.* Iron-containing pigment in the apparently characteristically pigmented skin was absent. 3. Cutaneous xanthomatosis with hypercholesteremia was present but diabetes was absent. 4. Deficiency in adrenal cortical and androgenic hormones was demonstrated at postmortem study. 5. The unusual cause of death, acute pancreatic necrosis, was apparently unrelated to the hemochromatosis.

Archives of Otolaryngology, Chicago

33:145-332 (Feb.) 1941

Diagnosis and Treatment of Tuberculosis of Larynx and Contiguous Areas. G. E. Wilson, Saranac Lake, N. Y.—p. 145.

Practical Points in Transconchal Radical Mastoidectomy. E. I. Matis, Kaunas, Lithuania.—p. 177.

*Prostigmine Methylsulfate in Treatment of Deafness and Tinnitus Aurium: Report of Fifty-Nine Cases with Negative Results. M. S. Ersner, I. A. Rush and D. Myers, Philadelphia.—p. 193.

Surgical Correction of Collapsed Alar Cartilages: Report of Case. C. E. Gurney, Portland, Ore.—p. 199.

Evaluation of Vertigo Following Head Injuries. S. Baumoel and M. I. Marks, Cleveland.—p. 204.

Thrombosis of Cavernous Sinus. E. Pace, Paducah, Ky.—p. 216.

Tuberculosis of Middle Ear and Mastoid. M. C. Myerson, New York, and J. G. Gilbert, Brooklyn.—p. 231.

Decubital Ulcers of Pharynx. R. Waldapfel, Grand Junction, Colo.—p. 251.

Primary Osteoma of Frontal Sinus. R. W. Teed, Ann Arbor, Mich.—p. 255.

Surgical Treatment of Bilateral Paralysis of Abductor Muscles. J. D. Kelly, New York.—p. 293.

Prostigmine Methylsulfate for Deafness and Tinnitus Aurium.—Ersner and his colleagues treated 59 cases of deafness and tinnitus aurium with prostigmine methylsulfate. Their results are contrary to those of their predecessors. The authors tested hearing with the audiometer and tuning forks. Tests were repeated twice a week. Four patients asserted that they had improved, but their audiometric readings disclosed no change. These patients said improvement continued even after administration of the drug was discontinued and physiologic solution of sodium chloride was substituted. Eighteen patients said that symptomatic improvement occurred soon after the first few injections, but here also improvement could not be verified by audiometer and tuning fork tests. After several weeks of treatment the euphoria and enthusiasm of the patients subsided, and the symptoms remained the same despite treatment. Eight patients after having received fifteen injections showed an 8 to 10 decibel improvement at varying times, but repeated hearing tests revealed that the improvement was neither permanent nor prolonged. Attacks of acute angina pectoris caused prostigmine therapy to be discontinued in 3 patients. The remaining *26* patients neither claimed nor showed any so-called improvement in the tinnitus aurium or hearing either during or after therapy.

Archives of Physical Therapy, Chicago

22:65-128 (Feb.) 1941. **Partial Index**

Climate and Weather in Relation to Physical Therapy. C. A. Mills, Cincinnati.—p. 69.

Uses and Abuses of Audiometers. C. E. Kinney, Cleveland.—p. 94.

Present Requirements for Acceptance of Hearing Aids as Determined by Council on Physical Therapy. H. A. Carter, Chicago.—p. 98.

Artificial Fever versus Combined Fever-Chemotherapy in Gonococcic Infections. H. W. Kendell, D. L. Rose and W. M. Simpson, Dayton, Ohio.—p. 103.

Bulletin of Johns Hopkins Hospital, Baltimore

68:119-202 (Feb.) 1941

John Jacob Abel: A Portrait. P. D. Lamson, Nashville, Tenn.—p. 119.
*Factors Influencing Plasma Prothrombin in the Newborn Infant: IV. Effect of Antenatal Administration of Vitamin K on Incidence of Retinal Hemorrhage in the Newborn. A. E. Maumenee, L. M. Hellman and L. B. Shettles, Baltimore.—p. 158.
Visceral Pain in Cases of Situs Inversus. A. B. King, Baltimore.—p. 169.
Pollen Survey of the Islands of Bermuda. L. N. Gay, H. Curtis and T. Norris, Baltimore.—p. 179.
*Lowering of Blood Uric Acid by Uricase Injections. Ella H. Oppenheimer, Baltimore.—p. 190.

Influence of Antepartum Vitamin K on Retinal Hemorrhage of the Newborn.—Maumenee and his associates point out that, although a few cases of true hemorrhagic diathesis with definite deficiency in the prothrombin have been reported, there has been no direct correlation between the prothrombin level of the blood and the incidence of neonatal hemorrhage. Since September 1939 the authors have given alternate mothers entering for delivery with a viable baby 2 mg. of menadione or a unit-equivalent vitamin K active substance. Fifty mothers in the treated series received an additional 2 mg. of menadione by mouth daily for at least four days before delivery. For six months the eyegrounds of all infants, with the exception of very premature ones, were studied for retinal hemorrhage. A total of 446 babies was examined; 173 were born to mothers who had received vitamin K during labor, 50 to mothers who had received prolonged vitamin K therapy and the remaining 223 to women who were not treated with vitamin K. In 26 infants with retinal hemorrhage, born of untreated mothers, the average plasma prothrombin level was 16.7 dilution units as against the average infant plasma prothrombin level of 28 dilution units. Babies with retinal hemorrhage then tend to show a diminished prothrombin level, but no direct correlation between the extent of the retinal hemorrhage and the degree of the hypothrombinemia could be demonstrated. The plasma prothrombin level of infants born to mothers receiving vitamin K was usually elevated. However, 21 such infants who had retinal hemorrhage showed an average prothrombin of 31 dilution units. Failure to promote a rise would seem to indicate either an extremely low prothrombin value before therapy, a resistance to intrapartum therapy or retinal hemorrhage early in labor; that is, before antepartum treatment. The latter is supported by hemorrhage in babies born by cesarean section performed during the early stages of labor. As the prothrombin levels of infants with hemorrhage born of untreated mothers are lower than in normal infants a reasonable explanation of retinal hemorrhage in this treated group would be one or a combination of the three foregoing factors. As intrapartum vitamin K may not provide complete prophylaxis against hypoprothrombinemia, 14 infants without retinal hemorrhage, whose mothers received vitamin K during labor, were picked at random for a control series. The average prothrombin levels of these infants were 44.6 dilution units. Only 2 of the infants of the 50 mothers who at term were given 2 mg. of menadione for at least four days and then labor was induced by artificial rupture of the membranes were found to have hemorrhages. Their prothrombin levels were 36.5 and 4.4 dilution units, respectively. The most probable explanation for this failure was a refractoriness of either the mother or the infant to vitamin K. The average level of 29 of the infants whose mothers were treated for at least four days was 56.1 units. Prothrombin studies done on mother and infant show that failure to respond to treatment with a vitamin K preparation was due to deficient absorption. Normal gallbladder studies indicated that this failure was not due to any abnormality of the biliary tract. Future studies may show whether or not this will be the explanation for all refractory cases.

Lowering of Blood Uric Acid by Uricase Injections.—Oppenheimer records the fact that a solution containing uricase if injected intravenously or intramuscularly into hens with a "gouty" or high plasma uric acid concentration will lower the uric acid level. The higher the plasma uric acid level, the greater the uricolytic activity of the enzyme. One determination of the duration of the uricolytic activity of a single uricase injection indicates that it lasts at least twenty-four hours. Two hens receiving weekly uricase injections for four and five weeks, respectively, showed a decidedly lower average uric acid level than control hens on the same meat diet. Determinations over longer periods are needed to establish the validity of the observation. The work has not been in progress long enough to determine whether the relatively small dosage of uricase employed will prevent the appearance of tophi.

Journal of Immunology, Baltimore

40:73-242 (Feb.) 1941. **Partial Index**

Anticoagulants and Complementary Activity: Experimental Study. E. E. Ecker and L. Pillemer, Cleveland.—p. 73.
Studies Concerning Possible Mechanisms Involved in Experimental Serum Sickness. L. R. Jones and E. C. Roberts, St. Louis.—p. 107.
Experimental Diphtheria in Albino Rat. E. Seligmann and C. W. Jungeblut, New York.—p. 119.
Studies on Mechanism of Arthus Phenomenon. P. R. Cannon and C. E. Marshall, Chicago.—p. 127.
Neutralization of Virus of Myxoma by Specific Immune Serum. R. F. Parker and L. H. Bronson, Cleveland.—p. 147.
Blood Groups of Papago Indians. E. L. Breazeale, R. A. Greene, Tucson, Ariz., and L. J. Kantor, Sells, Ariz.—p. 161.
Studies with Colored Antigens: I. Rate of Disappearance of Dye Albumin from Blood. H. N. Pratt and M. I. Gregersen, Boston.—p. 163.
Electrophoretic Analysis of Tetanal Antitoxic Horse Serums. J. van der Scheer, R. W. G. Wyckoff and F. H. Clarke, Pearl River, N. Y.—p. 173.
Active Immunization of Mice with Hemolytic Streptococci. J.-P. Wu, Peiping, China.—p. 179.
Staphylococcus Toxoid Prepared by Peptic Digestion. I. A. Parfentjev, Frances L. Clapp and A. Waldschmidt, Pearl River, N. Y.—p. 189.
Passive Immunization of Mice Against Human Influenza Virus by Intranasal Route. W. Henle, J. Stokes Jr. and Dorothy R. Shaw, Philadelphia.—p. 201.

Journal of Infectious Diseases, Chicago

68:1-96 (Jan.-Feb.) 1941. **Partial Index**

Studies on Virus of Psittacosis Cultivated in Vitro. H. Y. Yanamura and K. F. Meyer, San Francisco.—p. 1.
Therapeutic Properties of Sulfanilamide and Related Drugs in Experimental Typhoid Infection of Mice. R. T. Fisk, Los Angeles.—p. 20.
Laboratory Infections Due to Brucella. K. F. Meyer and B. Eddie, San Francisco.—p. 24.
Multiple Pneumococcic Infections in Pneumonia. Sarah L. Cockrell and J. M. Ruegsegger, Cincinnati.—p. 33.
Olfactory Mucosa as Possible Source of Antipoliomyelitic Substances. R. H. Allen and P. F. Clark, Madison, Wis.—p. 53.
Intracerebral Infection of Mice with Haemophilus Influenzae as Index of Strain Virulence and Protective Value of Immune Serum. Mercedes Vicente de Torregrosa and T. Francis Jr., New York.—p. 59.
Propagation of Virus of Lymphogranuloma Venereum on Chorioallantois of Developing Egg. M. E. Heward and Winifred S. Hull, New Haven, Conn.—p. 73.
Influenza Virus Studies During 1939 Epidemic in Central Europe. R. M. Taylor and M. Dreguss, Budapest, Hungary.—p. 79.
Certain Broad Epidemiologic Aspects of Influenza. R. M. Taylor, A. Petrilla and M. Dreguss, Budapest, Hungary.—p. 90.

Journal-Lancet, Minneapolis

61:35-68 (Feb.) 1941

Remote Vascular Lesions of Toxemias of Pregnancy and Their Clinical Significance. J. L. McKelvey, Minneapolis.—p. 35.
Appendicitis and Its Treatment. B. H. Brunkow, Billings, Mont.—p. 39.
Sterility Investigation: Plan for Study and Treatment. G. W. Hunter, Fargo, N. D.—p. 41.
Hypertension from the Standpoint of the Otolaryngologist. W. E. Camp, Minneapolis.—p. 45.
Thrombosis of Axillary Vein Following Effort: Case Report. R. N. Allin, Madison, Wis.—p. 47.
Cold Vaccine Study. L. L. Stanley, San Quentin, Calif.—p. 48.
Care of Acute Sinus. F. H. Roost, Sioux City, Iowa.—p. 49.
Recent Advances in Intravenous Fluid Therapy. J. H. Tillisch, Rochester, Minn.—p. 51.
*Use of Bacteriophage in Treatment of Furunculosis in Students. W. W. Dalitsch, Chicago.—p. 56.

Bacteriophage for Furunculosis.—Dalitsch states that furunculosis in students of the professional schools of the University of Illinois has been most prevalent in the spring. He believes that the treatment of furunculosis is incomplete without a wider use of bacteriophage. Friction of clothing along the collar line, sleeves and buttocks seems to favor inoculation of the skin. Trauma (picking the nose, plucking hair and squeezing of comedones) may initiate the lesion. Well nourished and obese persons are slightly more prone to this affliction. When the furuncle was in an early stage and the inflammation still diffuse with no opening into the lesion, hot water fomentations were applied continuously until pointing had occurred. The fomentations were covered with parchment

paper and held in place with adhesive tape. They were changed about every hour or two. When the lesion had sufficiently localized, the center of it was usually covered with a thin skin, and the lesion was opened by merely lifting off the desquamated tissue. A small wick drain, consisting of a few threads of plain gauze, was carefully passed into the sinus leading into the lesion and continuous wet dressings saturated with bacteriophage were applied. The bacteriophage dressing was covered with parchment paper and held in place with adhesive tape, with its upper margin left open. Bacteriophage was dropped on the dressing through the open upper edge in sufficient amount and often enough to keep it moist. In the case of intranasal infections a loose cotton dressing soaked with the bacteriophage was inserted into the nasal passage so as to be in contact with the infected area. At intervals additional bacteriophage was added with a medicine dropper to keep the dressing saturated. The technic is based on direct contact of the bacteriophage with the infected tissues. Plain gauze and cotton dressings were used because antiseptics hinder the action of bacteriophage. The students missed no time from classes. In a series of more than 200 cases encountered over five years the results were uniformly gratifying. Pain was relieved soon after the bacteriophage was applied. In from six to twelve hours the site of the lesion appeared much smaller, and tension and tenderness were greatly diminished. Thick purulent exudate was changed into a clearer serous drainage. Healthy granulations were soon evident. Movement of the affected part was possible, and dressings were changed without pain. The course of the infection was shortened and convalescence rapid. The method is particularly applicable to intranasal and facial infection. Every practitioner is familiar with examples of fatal complications resulting from these lesions. Intranasal furuncles present a type of infection that is always looked on with trepidation and helplessness because little active treatment can be used and because manipulation and instrumentation are contraindicated. The bacteriophage method gives a more effective active therapy from which prompt improvement can be expected with a high degree of confidence. "Crops" of satellite boils do not recur.

Journal of Pediatrics, St. Louis

18:145-288 (Feb.) 1941

Treatment of Pneumonia in Infants and Children. B. W. Carey, Detroit.—p. 153.
Sulfapyridine Resistance of Pneumococci Following Sulfapyridine Therapy in Infants and Children and Comparative Potency of Three Chemotherapeutic Agents for Pneumococci as Shown by Laboratory Tests. W. J. Anger, Toronto, Canada.—p. 162.
Dark Adaptation and Vitamin A: Further Studies with Biophotometer. P. C. Jeans, Evelyn L. Blanchard and F. E. Satterthwaite, Iowa City.—p. 170.
Comparison of Two Methods of Measuring Dark Adaptation. R. E. Eckardt and L. V. Johnson, Cleveland.—p. 195.
Absorption of Vitamin A in Celiac Disease: Interpretation of Vitamin A Absorption Test. C. D. May and J. F. McCreary, Boston.—p. 200.
Report of Clinical Experience with Meningococcic Meningitis. J. H. McLeod, Washington, D. C.—p. 210.
Meningococcic Meningitis: Role of Laboratory in Therapy. Sara E. Branham, Washington, D. C.—p. 217.
*Treatment of Hypoprothrombinemia (Hemorrhagic Disease) of Newborn Infant. R. B. Lawson, Chapel Hill, N. C.—p. 224.
*Histoplasmosis: Report of Case in Infant 3 Months of Age. P. H. Rhodes, Denver; N. F. Conant, Durham, N. C., and L. R. B. Glesne, Cincinnati.—p. 235.
Gangrene as Complication of Scarlet Fever: Report of Case with Panarteritis. A. L. Hoyne and L. Smollar, Chicago.—p. 242.
Postvaccinal Neuronitis: Report of Case. R. H. Young and C. Moore, Omaha.—p. 248.
Tongue-Tie in Infants and Children. E. T. McEnery and Frances Perlowski Gaines, Chicago.—p. 252.

Treatment of Neonatal Hypoprothrombinemia.—Lawson reviews the literature on the treatment of hypoprothrombinemia (hemorrhagic disease) of the newborn infant. He describes a microprothrombin test which makes repeated tests on infants safe and simple. The test is performed at the infant's bedside in a room with a temperature of not more than 80 F., by placing 20 cu. mm. of thromboplastin suspension in the well of a common, hollow-ground slide, using a 20 cu. mm. Sahli hemoglobin pipet. The infant's heel is washed with alcohol, dried and punctured with a sharp lancet so that the blood flows freely. Twenty cu. mm. of blood is drawn into a clean pipet, added to the thromboplastin and mixed with it for from five to ten seconds with a fine glass stirring rod. By tilting the slide, the mixture flows back and forth until a sharp end point occurs when it clots. The time is measured with a stop watch from the addition of the blood to the time of clotting and is expressed as the "microprothrombin time." The test can be performed repeatedly without danger to the infant. The author's studies show that the antepartum administration of menadione is effective in preventing hypoprothrombinemia of the newborn infant. It may prove desirable to give this drug or a similar naphthoquinone daily to mothers during the last month of pregnancy. If this has not been done, oral administration after labor has begun is effective if as much as 4 mg. is given at least five hours before delivery. Unless a decided degree of hypoprothrombinemia exists at birth, the intramuscular injection of 1 mg. of menadione in sesame oil during the first twelve hours of life will prevent any subsequent hypoprothrombinemia. Bile salts are not necessary for absorption in the newborn infant without biliary obstruction. Intramuscular blood transfusion is not effective prophylactically or therapeutically. The author considers a microprothrombin time of 75 seconds or longer as indicating a serious prothrombin deficiency.

Histoplasmosis.—Rhodes and his associates cite the occurrence of histoplasmosis in an infant of 3 months, evidently the youngest on record of the 5 cases reported. A culture of Histoplasma capsulatum was obtained from the infant's blood stream twenty-four hours before death. The incidence of the disease has risen sharply in the past two years. It should no longer be considered a rarity and must be ruled out whenever a leukopenia, prolonged fever, splenohepatomegaly, anemia of doubtful etiology or chronic infection of the respiratory tract is present. The symptomatology can vary, but a diagnosis may still be made by finding the small, oval, encapsulated organisms (from 1 to 3 microns) in the mononuclear cells in peripheral blood smears, sternal bone marrow smears, discharge from otitis media, sections of spleen removed at splenectomy and biopsy sections of skin and lymph nodes. The fungus, which is characterized by large warty, thick walled chlamydospores attached to the fungus filaments, is moldlike. No specific therapy has had sufficient trial because diagnoses, except for 3 cases, have not been made until necropsy. Further trial of antimony preparations—antimony and potassium tartrate and trivalent and pentavalent organic preparations of antimony—is advised.

Michigan State Medical Society Journal, Muskegon

40:81-160 (Feb.) 1941

Coronary Vascular Heart Disease. J. H. Musser, New Orleans.—p. 99.
Unusual Hypertension: Case of Ten Years' Duration. H. Stalker, Detroit.—p. 105.
Undescended Testis. L. J. Bailey, Detroit.—p. 107.
Congenital Umbilical Hernia with Eventration. H. M. Nelson and T. S. Fandrich, Ann Arbor.—p. 111.
Feminine Psychology, with Emphasis on Gynecologic and Obstetric Phases. L. A. Schwartz, Detroit.—p. 113.

New England Journal of Medicine, Boston

224:221-264 (Feb. 6) 1941

Sulfanilamide and Its Derivatives: Sulfanilamide in Management of Acute Streptococcic, Particularly Scarlatinal, Infections of Upper Respiratory Tract. C. Wesselhoeft, Boston.—p. 221.
Id.: Treatment of Puerperal Sepsis. J. P. Cohen, Boston.—p. 226.
Id.: Treatment of Urinary Tract Infections by Specific Therapy: Clinical Discussion. E. G. Crabtree, Boston.—p. 229.
Id.: Treatment of Meningococcic Meningitis. E. H. Place, Boston.—p. 234.
Id.: Skin Manifestations Due to Sulfanilamide and Its Derivatives. A. M. Greenwood, Boston.—p. 237.
Criminal Aspects of Faith Healing. I. H. Rubenstein, Chicago.—p. 239.
Uncommon Infectious Diseases in New England. C. S. Keefer, Boston.—p. 242.

224:265-306 (Feb. 13) 1941

*Studies on Hemoglobin Regeneration in Patients with Vitamin C Deficiency. E. L. Lozner, Boston.—p. 265.
*Sulfanilamide in Treatment of Acute Pelvic Inflammatory Disease. J. T. Williams, Boston.—p. 269.
Spinal Anesthesia in Obstetrics, Using Pontocaine-Glucose Solution. J. C. Shull and E. P. Manning, Boston.—p. 271.
*Diabetes Mellitus and Pregnancy. M. Nothmann, Boston.—p. 275.
Physiologic and Therapeutic Effects of Hypothermia. J. H. Talbott, Boston.—p. 281.

Hemoglobin Regeneration in Vitamin C Deficiency.—Lozner reports observations concerning hemoglobin regeneration in 5 patients with presumptive vitamin C deficiency (shown by complete chemical absence of reduced ascorbic acid from the

blood plasma) and moderate or mild anemia. The patients were treated with bed rest and a diet limited to whites of eggs, white bread, white soda crackers, butter, spaghetti, rice, bacon, corn syrup, tea, coffee and milk boiled for five minutes. Three of the patients presented the clinical picture of scurvy, 1 of pellagra and 1 of idiopathic hypochromic anemia. Four of the 5 patients showed satisfactory hemoglobin regeneration without vitamin C administration, even though on a diet containing only traces of vitamin C and vitamin B complex. In 3 of these 4 patients, the administration of ascorbic acid, after the initial hemoglobin regeneration, neither caused reticulocytosis nor increased the speed of hemoglobin increase. The remaining patient had clinical scurvy with melena and anemia. During the control period neither the melena nor the anemia disappeared. Coincident with vitamin C therapy the melena ceased, and reticulocytosis and hemoglobin regeneration ensued. Complete regeneration of hemoglobin of 2 patients did not occur until they were placed on yeast and a general diet.

Sulfanilamide for Acute Pelvic Inflammation.—Williams used sulfanilamide for the treatment of 72 patients who had acute pelvic inflammation. He compares the results with those obtained in 100 similar patients treated during the pre-sulfanilamide era by route bed rest, fluids, catharsis, ice or heat to the abdomen and hot vaginal douches. The patients given sulfanilamide received in all other ways the same treatment as the control series. There were no fatalities in either series. In the control series the temperature of 72 per cent of the patients fell to normal within one week after admission. Improvement of pain, tenderness and leukocytosis almost paralleled the fall in temperature. The average duration of the febrile reaction in the control series was six and seven-tenths days. The longest elevation of temperature elevation was thirty-five days. In 63 patients suffering from their first attack the average was seven and nine-tenths days; in 37 patients with recurrent attacks it was four and eight-tenths days. Seventy-two per cent of the sulfanilamide-treated patients also showed a normal temperature within one week. The average time for a normal temperature to appear was five and eight-tenths days. In primary attacks (44 patients) the temperature elevation averaged six days, whereas in recurrent attacks (28 patients) the average was five and seven-tenths days. The longest elevation of temperature was thirty-six days. This patient ultimately recovered after a pelvic abscess developed and broke through into the rectum just as she was being prepared for colpotomy. A pelvic abscess formed in another patient while she was under sulfanilamide treatment. It was drained by colpotomy on the seventh day after admission; the temperature fell to normal two days later. These 2 cases are regarded as absolute failures of sulfanilamide therapy. Of the control patients 13 per cent and of those treated with sulfanilamide 11 per cent were deemed to require salpingectomy. The dramatic results often obtained with sulfanilamide in streptococcic infections and with sulfanilamide and sulfapyridine in pneumonias were disappointingly absent.

Diabetes Mellitus and Pregnancy.—Nothmann states that 5 diabetic women with a past history of several abortions and stillbirths were successfully delivered by prophylactic cesarean section. The influence that pregnancy will have on the diabetes of the mother cannot be predicted in spite of careful treatment. Repeated pregnancies in the same patient may take different courses. The author describes a state of hypoglycemia in infants of diabetic mothers during the first days of life which is sometimes accompanied by periods of unconsciousness. Its cause is the hypertrophy and overfunctioning of the pancreas. The cholesterol level of the 5 newborn babies ranged from 58 to 74 mg. per hundred cubic centimeters. Only 1 baby had a value of 162 mg. An icterus neonatorum later developed in this infant. The children developed well and continued to be healthy. Considering the extremely high mortality rate that exists among the fetuses and children of diabetic women, prophylactic cesarean section is recommended to save the life of the fetus, whose life is in greater danger than the mother's.

New York State Journal of Medicine, New York

41:307-418 (Feb. 15) 1941

Arsenic as Possible Cause of Subacute Encephalomyelitis: Correlation of Chemical, Clinical and Histologic Observations. A. D. Ecker, Syracuse.—p. 335.
Nerve Pathways and Clinical Features of Shoulder Pain in Relation to Angina Pectoris. H. R. Miller, New York.—p. 345.
Some Problems Involved in the Fitting of Hearing Aids. T. H. Halsted and F. M. Grossman, New York.—p. 352.
*Periodontia in Internal Medicine: Periodontal Disease, Its Importance as Focus of Infection and Possibilities of Treatment. S. C. Miller and A. N. Arvins, New York.—p. 359.
Organization of an Arthritis Clinic, with Special Reference to the Arthritis Clinic at the Hospital for the Ruptured and Crippled, New York City. R. G. Snyder and C. Traeger, New York.—p. 365.
*Roentgen Ray Therapy of Plantar Warts. A. H. Montgomery and R. M. Montgomery, New York.—p. 371.
Early Recognition of Serious Lesions of Nose, Throat and Ear. G. M. Coates, Philadelphia.—p. 376.
Clinical Experiences with Stilbestrol. A. R. Abarbanel and M. D. Klein, New York.—p. 383.

Periodontia in Internal Medicine.—Miller and Arvins believe that the danger of internal infection from periodontal foci (pus pockets, gingivitis and the like) is much more potent than that from periapical disease. They list the following reasons: 1. A much greater zone is involved than in a periapical abscess, considering the total surface area of the walls of all pockets. At least twenty times the absorption surface is involved in an average case of periodontal disease as in a well developed chronic periapical abscess. 2. Absorption from the gingival crevice is more rapid, as the blood and lymph supply to the gingiva is much greater than to a periapical area in bone, especially when the latter is surrounded by even a slight degree of condensation. Round, Kirkpatrick and Hails have shown that the force of mastication is sufficient to pump bacteria and their toxins into the circulation. 3. Resistance to bacterial growth is lower in the gingival crevice than anywhere else in the oral cavity because of stagnation and food accumulation. The depths of gingival crevices and periodontal pockets offer an ideal incubation zone for strains of streptococci which grow best in a low oxygen environment. Therefore the authors point out that not only should any comprehensive search for foci of infection include roentgen evidence of lesions at the apexes of teeth but the study should encompass the alveolar margin for activity of bone destruction and a thorough clinical examination for gingival disturbances which have not as yet affected the bony structure. The amount of bone loss is not as significant as the type of bone which remains, for this determines the activity of periodontal disease. Periodontal disease is primarily dysfunctional in origin, and the disturbing factors producing a "locus minoris resistentiae" may be broadly grouped as functional, traumatic and systemic (endocrine, allergic and nervous). The primary therapeutic procedure is the restoration of functional coordination of the teeth so that stress is evenly divided and there is no strain in any excursive movements. In young persons orthodontia may be beneficial, in adults it should always be followed by the shaping of the teeth to conform to the patient's age and functional requirements. Dietary deficiencies or systemic diseases which may be causing or complicating the local disease must be attended to. The direct local requirement of a fibrous, detergent diet is of equal importance to the mineral, vitamin and other dietary requirements for oral health. Pus pockets must be eliminated by surgical gingivectomy, conservative surgery or conservative subgingival curettage. The etiologic factors of periodontal disease are rarely, if ever, single. Periodontal disease can be cured, and the resulting improved health can be maintained.

Irradiation for Plantar Warts.—The Montgomerys report the results of treating 583 patients with plantar warts exclusively by means of roentgen rays. Of the 487 patients whose end results are known, 439 or 90.35 per cent were cured. Mosaic warts with ill defined edges, which they have found radioresistant or unsuitable for close shielding, were not included. Otherwise the cases were unselected. Most of the warts had resisted other forms of treatment or they were recurrences. Many were fibrosed and their average duration was eleven months. A radical modification of the usual technic was employed. It consisted of a large predetermined initial

dosage, its size depending on several factors (size, depth, callus, keratitis and fibrosis), followed at intervals of ten days by one, two or three saturation doses of four fifths that of the initial dose, through precisely fitting shield holes in lead sheeting. These holes are reduced in size as the lesion shrinks. There were no reactions, pain, loss of time from work or any other unfortunate sequelae. Seldom have the authors irradiated a wart previously treated by others with radium or roentgen rays, for even if the total dosage given is known the size of the aperture through which the irradiations had been given is seldom definite.

North Carolina Medical Journal, Winston-Salem

2:59-108 (Feb.) 1941

Sulfathiazole in Treatment of Severe Staphylococcic Infection. W. B. Martin and R. B. Grinnan Jr., Norfolk, Va.—p. 59.
The Art of Pediatrics. S. F. Ravenel, Greensboro.—p. 63.
The Science of Pediatrics. D. L. Smith Sr., Saluda.—p. 65.
Pediatric Economics. R. W. Roberts, Durham.—p. 67.
The Aims of the American Academy of Pediatrics. A. H. London Jr., Durham.—p. 71.
Mortality with Causes of Death in Series of 917 Consecutive Hysterectomies. E. S. Boice, Rocky Mount.—p. 72.
Pneumoconiosis. H. F. Easom, Sanatorium.—p. 79.
Prolonged Occlusion in Latent Phorias. F. O. Fay, Norfolk, Va.—p. 83.
Full Term Intra-Abdominal Pregnancy: Report of Case. R. A. White, Asheville.—p. 87.

Radiology, Syracuse, N. Y.

36:131-260 (Feb.) 1941. **Partial Index**

Oral Cholecystography: Basis of Standardization of Method. W. W. Robinson, Memphis, Tenn.—p. 131.
Craniolacunia (Lückenschadel): Report of Fifty-Four Cases. E. C. Vogt and G. M. Wyatt, Boston.—p. 147.
Importance of Accurate Collimation of Beam in Deep Roentgen Therapy: Effect of Size of Focal Area and Position of Limiting Diaphragm, with Special Reference to Supervoltage. E. Schons, St. Paul.—p. 154.
Roentgen Localization of Myocardial Damage Resulting from Coronary Artery Disease. G. Levene and R. M. Lowman, Boston.—p. 159.
Aneurysm of Splenic Artery. J. V. Seids and H. Hauser, Cleveland.—p. 171.
Systemic Care of Patients Undergoing Radiation Therapy. J. D. Peake, Mobile, Ala.—p. 181.
Induction by Roentgen Rays of Hereditary Changes in Mice. G. D. Snell, Bar Harbor, Maine.—p. 189.
Roentgen Diagnosis of Neoplasms of Air and Food Passages, with Particular Reference to Larynx. E. P. Pendergrass and B. R. Young, Philadelphia.—p. 197.
The Copying of Roentgenograms. G. M. Busanovich, Philadelphia.—p. 212.
*Peptic Ulcer: Review of 1,033 Cases and Follow-Up Study of Patients Diagnosed Between Ten and Twenty Years Ago. M. F. Dwyer, J. M. Blackford, W. A. Cole and R. H. Williams, Seattle.—p. 217.
Slight Enlargement of Head of Pancreas: Associated Pathologic Changes in Duodenum: Report of Seven Cases. M. Feldman, Baltimore.—p. 224.

Peptic Ulcer.—Dwyer and his associates review the 930 cases of duodenal ulcer and 103 cases of gastric ulcer encountered in a private clinic up to January 1939. In order to determine the progress of the patients with duodenal ulcer they sent out questionnaires to 238 patients who had been treated medically and surgically for ulcer from ten to twenty years before. Responses were received from 141 patients, 77 of whom had received medical and 64 surgical treatment. The average time since treatment had been fourteen years. Tabulation of the results for the 77 patients who had received medical treatment showed that 65 per cent considered themselves as having obtained 75 per cent or more relief of their gastric symptoms. Approximately one third (35 per cent) of the medically treated patients stated that they had obtained only 50 per cent or less relief of their symptoms and one half (56 per cent) of the patients with unsatisfactory results were later operated on. Pyloric obstruction developed in 6 per cent of the medically treated patients in an average of ten years. Of the 64 patients treated surgically, 86 per cent considered that they had received 75 per cent or more relief from their symptoms after operation. Posterior gastroenterostomy was done on 52 of these patients, and satisfactory results were obtained in 90 per cent; pyloric obstruction was the indication for operation in only 6 patients. The ulcer was excised in the remaining 12 patients and, after ten years, only one third considered the operation a success. Hemorrhage was recorded in 208, or 19 per cent of the entire series. Active hemorrhage caused 113 of these patients to seek relief. Massive hemorrhage is more frequent before 45 years of age, but vital statistics show that only 4 per cent of patients dying of massive hemorrhage from peptic ulcer are less than 45 years of age. Early emergency operations for massive hemorrhage from ulcer in patients more than 45 years of age should save many lives. The highest incidence of duodenal ulcer is between 21 and 30 years of age; one third of the authors' patients began to have dyspepsia during this decade. The younger the patient at the onset of duodenal ulcer, the more characteristic are the symptoms. Patients less than 30 years of age who present gastric symptoms suggestive of peptic ulcer are more apt to have an ulcer than are older patients, especially those more than 40 years of age. The causes of reflex manifestations are considerably less frequent in younger patients than among older ones. Careful roentgen examination is the most important factor in diagnosing or excluding duodenal ulcer. Gastric ulcer is found in relatively older persons. The symptomatology of gastric ulcer often presents atypical and irregular disturbances, and these tend to be more severe than those associated with duodenal ulcer.

Southwestern Medicine, El Paso, Texas

25:35-66 (Feb.) 1941

Lung Tumors. C. W. Maynard, Pueblo, Colo.—p. 35.
Treatment of Generalized Peritonitis. D. C. Collins, Los Angeles.—p. 39.
Infections of Head and Neck. G. L. Pattee, Denver.—p. 41.
Recent Advances in Surgery. E. P. Palmer, Phoenix, Ariz.—p. 43.
Incidence of Syphilis Among College Students. R. A. Greene, E. L. Breazeale and J. E. Andes, Tucson, Ariz.—p. 46.

Surgery, St. Louis

9:163-330 (Feb.) 1941

Jejunostomy for Relief of Malfunctioning Gastroenterostomy Stoma. A. W. Allen and C. E. Welch, Boston.—p. 163.
Section of Spinothalamic Tract in Medulla with Observations on Pathway for Pain. H. G. Schwartz and J. L. O'Leary, St. Louis.—p. 183.
Wound Healing, with Especial Reference to Muscle and Fascia Repair. K. S. Chouké, Philadelphia, and R. W. Whitehead, Denver.—p. 194.
*Management of Postoperative Wound Separation. L. S. Fallis, Detroit.—p. 198.
*Postoperative Shock Due to Hemolytic Streptococcus Wound Infection. J. D. Stewart, Boston.—p. 204.
Oral and Parenteral Use of Synthetic Vitamin K Active Substances in Hypoprothrombinemia. J. D. Stewart, Boston.—p. 212.
Relative Merits of Scalpel and High Frequency Current in Nephrotomy: Experimental Study. C. C. Higgins and M. Glazier, Cleveland.—p. 220.

Management of Postoperative Wound Separation.—Fallis suggests that conservative nonoperative treatment be more widely adopted for treating disrupted abdominal wounds. A review of all the cases of such wounds at the Henry Ford Hospital up to and including the year 1935 gives the mortality rate of 34 per cent; 70 per cent of the patients who died did so within twenty-four hours of being subjected to secondary closure. It seems that at least in certain cases the operation itself was a determining lethal factor. Therefore alternative methods of management should receive serious consideration. Since 1936, 27 cases of wound disruption have been treated; they occurred among 4,153 laparotomies. The mortality rate was 37.3 per cent; but what is significant is the evidence in favor of nonoperative treatment. Seven of the 16 patients whose wounds were resutured died, a mortality of 43 per cent, but only 3 of the 11 whose wounds were strapped with adhesive tape died, a mortality of 27.3 per cent. Henceforth the author states that secondary suture has gradually been abandoned until, in the last two years, all disrupted wounds occurring in the general surgical service of the Henry Ford Hospital have been treated by packing and adhesive strapping, with excellent results.

Postoperative Shock Due to Hemolytic Streptococcus Wound Infection.—Stewart reports 4 cases which illustrate the syndrome of postoperative shock due to fulminating infection of the operative field with hemolytic streptococci. There was a delay of more than twenty-four hours after the onset of shock before wound infection was suspected. Immediate recognition is urgent, so that specific chemotherapy and immunotransfusion may be initiated early.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

53:33-64 (Feb.) 1941

*Effects of Sulfonamide Compounds on Lupus Erythematosus. H. W. Barber.—p. 33.
Physical Properties of Ointment Bases. P. B. Mumford and R. M. Mumford.—p. 45.
The Carrot as a Cause of Dermatitis. H. R. Vickers.—p. 52.

Sulfonamide Compounds and Lupus Erythematosus.—Barber suggests that lupus erythematosus may be of either tuberculous or streptococcic origin. When of the latter origin, sulfonamides (usually sulfanilamide) destroy the streptococci in the various foci and liberate toxin which provokes a complex reaction consisting of a rise of temperature, usually preceded by a rigor of varying intensity, generalized or localized pains in the fibromuscular tissues, a widespread scarlatiniform erythema, a focal reaction in existing patches of the eruption, reactivation of healed patches, appearance of new erythematous lesions continuous with or distinct from areas already affected, and painful swelling of lymph nodes. When the reaction has subsided, the eruption improves or disappears because of the diminished absorption of toxin or antigen. Although subsequent administration of the drug may be followed by an immediate and severe reaction, possibly owing to the remaining organisms being more vulnerable or accessible to it, the reactions tend progressively to diminish as the organisms are gradually destroyed. When a tuberculous infection was apparently responsible, the reactions did not occur nor was the eruption affected. The author believes that the reactions are due to the liberation of streptococcus toxin by the action of the sulfonamides on latent foci of infection and are not instances of drug fever.

British Journal of Ophthalmology, London

25:49-96 (Feb.) 1941

Chi Square Test of Significance Applied to Series of Intracapsular Cataract Extractions. W. J. B. Riddell.—p. 49.
*Experimental Pigmentary Degeneration of Retina by Sodium Iodate. A. Sorsby.—p. 58.
Nature of Experimental Degeneration of Retina. A. Sorsby.—p. 62.
Convergence. Margaret Dobson.—p. 66.
Third Brazilian Congress in Ophthalmology, July 1939. E. E. Cass. —p. 71.

Experimental Pigmentary Degeneration of Retina by Sodium Iodate.—Sorsby reviews clinical cases in which the use of septojod (a German iodine preparation containing sodium hypoiodite and sodium hypoiodate) led to transient or permanent loss of vision from pigmentary retinal changes. The author's experimental work and that of others leading to the incrimination of sodium iodate as the toxic agent is presented. The dosage for the experimental production of pigmentary degeneration of the retina in the rabbit is 5 cc. of 2 per cent solution injected intravenously. There is no evidence that with this dosage there is any permanent damage to other tissues, so that sodium iodate may be regarded as a selective poison for the retina. Vital staining (with Kiton fast green) has shown that the retina is damaged by iodate in the albino rabbit though no pigmentary disturbances are seen with the ophthalmoscope. Septojod has been used widely in German-speaking countries for septic conditions on the assumption that nascent iodine is liberated in the presence of septic material. It has been especially popular in the treatment of puerperal sepsis.

British Journal of Radiology, London

14:79-114 (March) 1941

Cysticercus Cellulosae: Its Radiographic Detection in the Musculature and Central Nervous System. J. F. Brailsford.—p. 79.
Radiologic Investigation of Dyspeptic Soldiers. R. Saffley.—p. 96.
Comparison of Effects of Neutron and Gamma Ray Ionization on Electrophoretic Mobility of Colloidal Graphite Particles. L. H. Gray, J. Read and H. Liebmann.—p. 102.
Combination of Cholecystography and Barium Meal Examination: Economical and Practical Value. A. S. Johnstone.—p. 107.
X-Ray Skin Reactions and Protective Role of Normal Tissues. B. Jolles. —p. 110.
Symptomatic Leukemia. H. G. Hadley.—p. 113.

Rassegna Internazionale de Clinica e Terapia, Naples

21:769-808 (Nov. 15) 1940. **Partial Index**

*Placental Extract in Exanthematic Diseases. M. Bassi.—p. 771.
Test of Galactosuria in Diagnosis of Function of Liver in Calculous Cholecystitis. P. Emiliani.—p. 783.

Placental Extract in Exanthematic Diseases.—Bassi employed placental extract treated with phenol for prevention of measles in 192 children. All but 4 proved to be immunized. Measles was mild in the 4 children who had it. One child who was not given the preventive injection because she stated that she had had the disease acquired it. The author administered this treatment to 7 young adults with scarlet fever, measles or varicella. The extract was given intramuscularly in daily doses of 4 or 5 cc. for three or four days. The course and duration of the disease were mild in all the patients. The author believes that placental extract is of preventive and therapeutic value in exanthematous diseases. The earlier the treatment the better the results. The treatment attenuates the disease and prevents complications.

Klinische Wochenschrift, Berlin

19:1153-1176 (Nov. 9) 1940. **Partial Index**

Range and Technic of Serodiagnosis of Tuberculosis. K. Beller.—p. 1153.
*Hepatic Cirrhosis and Hepatargy on Allergic Basis. F. E. Schmengler. —p. 1155.
Question of Centrally Conditioned Disturbances of Cardiac Rhythm (Temporary Extrasystole in Internal Hydrocephalus). F. Brauch. —p. 1157.
Prevention of Serum Disease: Study of Problem of Immunity. E. A. Voss.—p. 1159.
Histamine Content of Blood of Smokers. E. Werle and G. Effkemann. —p. 1160.
Alteration of Reaction of Organism in Experimental Eczema. F. Koch and H. Buchwald.—p. 1162.
Short Wave Cardiography a New Method for Clinical Examination. L. Rósa.—p. 1163.
Behavior of Aneurin (Thiamine) and of Pyrophosphate of Thiamine (Cocarboxylase) in Blood in Tolerance Test with Vitamin B1. S. Molnár and M. Horányi.—p. 1165.

Hepatic Cirrhosis and Hepatargy on Allergic Basis.—According to Schmengler's investigations the liver is involved in all processes which develop on the basis of a general allergic reaction. The symptom of this involvement can be demonstrated in a large percentage of cases of urticaria, Quincke's edema, rheumatism, serositis and polyserositis, asthma, acute glomerular nephritis, scarlet fever and some cutaneous diseases. Usually the hepatic damage is latent and without much significance. In some cases it is so pronounced as to overshadow all other symptoms. Since sensitization of the liver can be brought about by way of the portal circulation as well as by the systemic circulation, allergic injury of the liver can be caused by infectious foci as well as by disturbances in the gastrointestinal tract. Hepatic cirrhosis can be produced not only by alcohol but also by various toxins, which indicates that the development of this disease must also be possible on the basis of an anaphylactic reaction. It has been suggested that the so-called serous hepatitis might be the hitherto unknown first stage of hepatic cirrhosis. The author reports 2 cases which he regards as proof that hepatic cirrhosis might develop on the basis of an antigen-antibody reaction. The first patient was subject to hay fever and asthma. The hepatic impairment here was demonstrated by a severe disturbance in the galactose tolerance and a strongly positive Takata reaction. The second patient repeatedly developed severe urticaria after eating fresh fish. One severe and prolonged attack of urticaria was finally controlled by a strict diet. The patient then completely abstained from fish and was free from urticaria. Three weeks before the present hospitalization she had again eaten fish and on the following day she had a recurrence of urticaria, nausea and vomiting. Jaundice developed, and the skin had become a dark greenish yellow. The general condition became greatly impaired, and the patient died in coma. Necropsy disclosed cirrhosis. Nature has provided in these 2 cases more convincing proof than could be furnished by artificially induced experiments. Katsch once observed acute yellow necrosis of the liver following urticarial mani-

festations on the skin, but he failed to provide an explanation. The 2 cases reported here prove that serous hepatitis, latent liver damage, cirrhosis of the liver and hepatargy are a pathogenic and etiologic unit developing on the basis of a repeated allergic impairment.

Medizinische Klinik, Berlin

36:1123-1150 (Oct. 11) 1940. **Partial Index**

Estimation of Articular Lesions. E. Güntz.—p. 1123.
*Bechterew's Spondylarthritis Ankylopoietica with Special Reference to Incipient Stages and Atypical Forms. M. Eltze.—p. 1125.
Duodenal Ulcer and Iron Metabolism: Symptomatic Erythrocytosis. K. Hitzenberger and W. Blumencron.—p. 1131.
*Thrombopenic Hemorrhages After Repeated Administration of Sedormid. H. Schäfer.—p. 1133.

Bechterew's Spondylarthritis Ankylopoietica.—Eltze reviews the pathologic anatomy and then describes the clinical picture of completely developed ankylopoietic spondylarthritis. Since early recognition is of great importance for effective treatment, he gives special attention to the incipient stages. The disease is sometimes preceded by rheumatic purpura or by nodose rheumatism of the scalp. An iritis may be the clinical sign of rheumatism. Neuralgias in the sciatic nerve, particularly if they are bilateral, and prolonged pain in the back make it advisable to resort to roentgenoscopy of the pelvis. This will frequently disclose changes in the sacroiliac articulation. The articular clefts are indefinite, and the articular surfaces appear as if gnawed on. Inflammatory niches are interspersed with narrow bone bridges, which gradually become wider. Cloudy densifications of the bone appear near the articular clefts. From one to three or even more years may elapse before these changes become visible in the roentgenogram. Limitation of the respiratory excursion likewise may occur early. The sedimentation speed of the erythrocytes is nearly always increased during the early stages. The rigidity of the vertebral column should make the observer think of ankylopoietic spondylarthritis. In the severe forms, complete stiffening and ossification take place within a few years or a decade and the patients become completely helpless. The benign form develops more slowly, in that two decades may elapse before the patient becomes incapacitated; the stiffening is usually not so severe in these cases. The atypical forms of ankylopoietic spondylarthritis are characterized by the fact that not only the large joints near the trunk (shoulder and hip joints) are diseased but also the more distal ones, that is, the elbow, hand, finger, knee and foot joints. Rheumatic heart disease may also exist. The recognition of the atypical forms is difficult because the clinical symptoms are often slight in spite of chronicity. However, if Bechterew's spondylarthritis ankylopoietica is thought of and sought, diagnosis is possible, particularly if the vertebral column is held rigid and the sacroiliac joint exhibits changes. To differentiate ankylopoietic spondylarthritis from spondylosis, it should be considered that spondylosis is due to wear and develops in persons of advanced age, whereas ankylopoietic spondylarthritis develops in the second or third decade of life although it may remain long unrecognized, so that it is not diagnosed until spondylosis causes the first complaints. Spondylarthritis ankylopoietica involves the entire or large portions of the vertebral column, whereas spondylosis is limited to a few vertebrae. There is no flattening of the physiologic lumbar lordosis, no increase in the sedimentation speed of the erythrocytes and no change in the sacroiliac joint in patients with spondylosis. The bridge formations on the vertebrae are thick in spondylosis, thin and shell-like in ankylopoietic spondylarthritis. The vertebral bodies are of glass-like transparency in ankylopoietic spondylarthritis, whereas their density is rather increased in spondylosis.

Thrombopenic Hemorrhages After Sedormid.—Schäfer reports the histories of 2 patients who developed thrombopenic hemorrhages after taking the hypnotic preparation sedormid (allyl-isopropyl-acetyl-carbarmide). One case had a relatively mild course. In this case two tablets were necessary to elicit the symptoms, whereas in the other case a single tablet produced severe and prolonged hemorrhages and disturbances in the general condition. The thrombopenic hemorrhages produced by sedormid usually terminate in complete cure, but if the physician does not know of the intake of this hypnotic he may diagnose a true thrombopenia. The author deplores the fact that sedormid in contradistinction to other, probably less harmful, barbituric acid hypnotics is obtainable without prescription. The author thinks that the firm marketing this hypnotic should at least be obliged to declare on the label the possibility of the development of hemorrhages of the skin and the mucous membranes.

Zeitschrift f. d. ges. Neurol. u. Psychiatrie, Berlin

170:131-282 (Aug. 27) 1940

Aspects of Diffuse Cerebral Sclerosis: Case of Familial, Late Infantile Type. O. Brandberg and E. Sjövall.—p. 131.
*Question of Ovarian Insufficiency in Mothers of Children with Mongolian Idiocy. H. Schröder.—p. 148.
Epileptic Aura. W. C. Weber and R. Jung.—p. 211.

Ovarian Insufficiency in Mothers of Children with Mongolian Idiocy.—Schröder studied sixty families in which mongolian idiocy occurred and obtained from the mothers detailed personal data on menstruation, the course of the pregnancy and birth of the mongolian idiot, gynecologic disorders and systemic diseases. After presenting the casuistics, he discusses such factors as belated menarche, disturbances of the menarche, persisting menstruation during pregnancy, disturbances in the menstrual cycle, ovarian and other gynecologic disorders, the menopause, signs of incretory disturbances and general diseases. Summarizing his observations he says that less than one fifth (11 of 60) of the mothers of children with mongolian idiocy had indications of an ovarian insufficiency in connection with the pregnancy resulting in the birth of the mongolian idiot. Control investigations on 60 mothers of normal children revealed similar disturbances in 18 cases at the time of conception or during gestation. Thus ovarian insufficiencies are of, not more than average frequency in mothers of mongolian idiots. The author reaches the conclusion that Geyer's hypothesis, which ascribes the development of mongolian idiocy to the fertilization of ova the plasm of which had been impaired because of ovarian insufficiency in the mothers (dysplasmatic ova), cannot be corroborated.

Jahresb. d. Kurashiki-Zentralhosp., Kurashiki

15:1-94 (Dec.) 1940. **Partial Index**

*Influence of Deuteron-Deuteron-Neutron Rays on Blood Picture of Rabbits. H. Tatiiri and H. Ueda.—p. 35.

Deuteron-Deuteron-Neutron Rays and Blood Picture.—Tatiiri and Ueda report their observations on the changes in the blood picture of rabbits treated with deuteron-deuteron-neutron irradiation, which contains no gamma rays, and compare the effect thus obtained with that of radon-beryllium rays containing the gamma rays. The source of these radiations was the Nonaka modification of the Cockcroft-Walton apparatus, and the irradiation was given over the epigastrium of the animals for periods varying from five to sixty minutes at a distance of 10 cm. As a rule the principle effect of the irradiation was a significant diminution of white blood cells, a left shift of the pseudoeosinophilic granulocytes and a particularly striking destruction of lymphocytes. Initial leukocytosis was observed in animals receiving irradiation for short durations (five to twenty minutes) but never in animals receiving longer intervals of irradiation (forty to sixty minutes). This constitutes proof of the fact that the neutrons, like other rays, obey the law of Arndt-Schulz. In comparison with the influence of radon-beryllium irradiation, the authors note one decided difference, namely that radon-beryllium irradiation exerts a much greater effect on the lymphocytes than does comparable amounts (millicurie units) of either the neutrons or the gamma rays from radon, but not more so than the combination of the two. This can mean only that the destructive effect of the radon-beryllium rays on the leukocytes results not merely from the simple summation effects of neutrons and gamma rays but from a complicated and synergistic effect of the two kinds of rays.

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Opportunities for Surgeons in Medical Research

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CHICAGO

The most important opportunity, which, indeed, I would call an obligation and privilege, of the Society of University Surgeons is the participation in surgical research by its individual members. But first let me emphasize that I do not imply that every member must do research. It is well that our membership includes a variety of surgeons. Though surgeons have contributed much they have perhaps the rare and shameful distinction of having hardly a single society organized for the primary purpose of scientific investigation. The internists have two or three societies designed almost solely for the purpose of research; one of them, the Central Society for Clinical Research, benevolently maintains a small quota of their membership for surgeons. All of us are aware of the necessity for research in the progress of surgery. Since the membership of the society contains men all of whom are in the so-called age of research productivity, and since it is made up of men engaged in academic activities, it becomes imperative that we concentrate on research.

To emphasize still further the importance of research let me refer to some quotations by the physiologist Claude Bernard. With the exception of Pasteur, no man has been responsible for more rapid strides in medicine, in an equivalent length of time, than Bernard. The book he wrote in 1865 on Experimental Medicine, which was translated into English in 1927, is a masterpiece on the philosophy of research and cannot fail to inspire any of us. If you have not read it, I would urge you to do so. You will find it a splendid antidote for that depressed feeling which follows a day when all experiments go wrong and nothing seems to have been accomplished. There is one danger, however, which the reader must fight against in reading this volume: he must take care lest the brilliance yet simplicity of Bernard's reasoning inflict on him an inferiority complex. Bernard presented medicine with so many illustrious advances only because he began his contributions early and persisted in his endeavors during even the latter days of his sixty-five years of life.

Early in his book it is obvious that Bernard wants it to be clearly understood just how important research is to progress in medicine; he remarked "Experimentation is undeniably harder in medicine than in any other science; but for that very reason it was never so necessary, and indeed so indispensable. The more complex the science, the more essential it is, in fact, to establish a good experimental standard, so as to secure comparable facts, free from sources of error. Nothing, I believe, is today so important to the progress of medicine." He repeats these thoughts, in different words, in many places throughout the book, thereby clearly indicating his belief in the importance of research work to medical science. He paid tribute to the great men of science by remarking that "It is in the darker regions of science that great men are recognized; they are marked by ideas which light up phenomena hitherto obscure and carry science forward." Yet he offered some slight solace to those of us outside the classification of great men by adding "Mediocre men often have the most acquired knowledge."

Although it is a well known fact that comparatively few men have the mental attributes to be successful research men, it is equally well known that men may be very intelligent without having the knack of being proficient in research. While originality is one of the most important attributes necessary, many additional characteristics indeed are required to produce men like Bernard and Pasteur. No more than two or three such geniuses will be encountered in any single century. There is great danger in attaching too much importance to originality, since a man with perseverance and industry, though lacking originality, is more apt to be productive (particularly if well guided) than a man displaying originality but lacking the tenacity to complete a long problem.

Part of the Presidential Address Delivered at the Third Annual Meeting of the Society of University Surgeons, St. Louis, Feb. 14, 1941.

Innumerable characteristics are therefore desirable and even necessary in the successful experimentalist. An astute power of observation is important indeed as exemplified by Bernard's story of his discovery of the relationship of the pancreas to fat digestion. He was operating on some rabbits while working on another problem when he discovered that white milky lymphatics were visible on the lower part of the duodenum beginning at about the point where the pancreatic duct emptied into the duodenum. More direct experiments dealing with the action of pancreatic juice on fats proved the suspected role of pancreatic juice in fat digestion. This experiment successfully illustrates how related or side problems may be much more important than the original problem. All of us have seen plenty of examples of this truth and in fact have had it happen to us. Unfortunately, these side problems can chase one up blind alleys at an amazing rate of speed, as most of us can again verify. Even the wary eye of a wild duck can be deceived by a dab of color properly placed on a wooden decoy. I hope none of you have been deprived of the pleasure of first hand experience in the demonstration of that phenomenon.

To get the most out of experimental work, one must at all times be an opportunist. Offhand, we might think that none of us would fail to take advantage of an opportunity when encountered in our path. Yet the old master himself (Bernard) pays a kindly tribute to William Beaumont for having the foresight to turn circumstances to profit when Alexis St. Martin came to him with a hole in his stomach.

Failure to interpret results accurately is a frequent error and destroys the significance of many a problem. Too often indeed does the experimenter let coincidence lead him astray into fields of thistles and cactus. Bernard wrote that "coincidences form one of the most dangerous stumbling blocks encountered by experimental scientists in complex sciences like biology. It is the *post hoc, ergo propter hoc* of the doctors, into which we may very easily let ourselves be led, especially if the result of an experiment or an observation supports a preconceived idea." The latter mistake is equally important and common. Bernard consumes no less than thirty pages in condemning the habit of starting on the dangerous mission of proving a preconceived idea. Variations in results are the bugbear of all scientists. However, Bernard took pains to issue a warning as follows: "Nothing is accidental, and what seems to us accident is only an unknown fact whose explanation may furnish the occasion for a more or less important discovery." It was utilization of this philosophy that led Bernard to the discovery of the role of the liver in carbohydrate metabolism with conversion of glycogen to sugar and vice versa. He found wide variations in his analyses of the sugar content of animals' liver; these variations consisted chiefly of higher readings several hours after removal of the liver from the body than at the time of removal. It was because he had faith in his analyses and repeated the experiments many times that he finally demonstrated without question the role of the liver in carbohydrate metabolism.

Scientists are continually being criticized for working on problems and issuing reports with doubtful value. Yet Bernard often makes the statement that there is no such thing as an unsuccessful experiment. He voiced my feelings exactly in his remarks, which cannot be improved on: "I therefore refuse to acknowledge that science has a place for men who make criticism their specialty, as in letters and in the arts. To be really useful, criticism in every science must be done by men of science themselves, and by the most eminent masters." In other words, no one knows at what time certain seemingly trivial data may be picked up by an opportunist and crystallized into an epoch making discovery by utilizing some additional data. After all, does it not seem a far cry from Dam's experiments on a bloody diarrhea in chicks, or Roderick's demonstration of hepatic disease in sweet clover disease of cattle, to the development of vitamin K? Perhaps it does, yet these two insignificant experiments gave rise to the dramatic and useful discovery of prevention of hemorrhage in jaundice. All of us, when we stop to think, can recall to mind many such instances when major discoveries were made possible by some trivial, seemingly insignificant, experiment.

Medical scientists fully realize that animal experimentation is a much better medium for development of important data than a flock of test tubes and inorganic bodies. It is likewise granted that the human being is a much better guinea pig than the four legged genus Cavia porcellus himself. We must realize, however, that while we are finding 8 or 10 patients with the proper symptom complex we might have completed a hundred or more experiments on animals, thereby tending to eliminate the statistical error of the time worn apology "a small series." Moreover, we must constantly ask ourselves that simple question Are my experiments jeopardizing the patient's health or chance of recovery? Again, Bernard touched the crucial point when he said "The principle of medical and surgical morality therefore consists in never performing on man an experiment which might be harmful to him to any extent, even though the result might be highly advantageous to science, i. e., to the health of others. But performing experiments and operations exclusively from the point of view of the patient's

own advantage does not prevent them turning out profitably to science."

The young ambitious medical scientist, more saturated perhaps with the vision of glory than with the persevering, analytic astuteness of a seasoned scientist, may in desperation and disgust say "Why work any more; all discoveries of importance have already been made?" Of course, we are all aware of the fallacy of that remark and realize that the addition of scientific facts as compiled year after year increases the chances of development of epoch making discoveries in a geometric ratio. True enough, the chances of making epochal discoveries in the mechanics of operative principles are being diminished; not so though with the physiologic principles involved in operations. Still more fruitful are the physiologic principles which can be utilized for the patients' welfare before or after operative procedures are performed.

As all of us fully realize, the benefits derived from the practice of medicine or surgery may be threefold: (1) personal satisfaction or happiness, (2) financial reward and (3) creation of an enviable professional reputation. All of the peers and seers of medicine as far back as the hippocratic era remind us of the serious accusations hurled at the monetary instinct. It is axiomatic that indeed few surgeons of the academic group (exemplified by this society) chose that path for the monetary compensation obtainable. Naturally, they elected to spend the majority of their time in institutional work for the personal satisfaction derived from work itself or the reputation created. I have no doubt that all the members of this audience are well aware of the curious fact that the short cut to an enviable national reputation lies in the corridors which traverse the halls of experimental medicine and surgery. The esteem of one's fellows, beyond his local environs, can be achieved in about half the time required by concentration on purely clinical medicine or surgery. It is likewise self evident that because of his lasting contributions to mankind this type of doctor will always be in demand. May his kind flourish and prosper!

1853 Polk Street.

The Function of the Museum in the Medical School

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Various types of museums find their place in the medical school. The chief of these are the anatomic museum and the pathologic museum. It is with the latter that this paper deals. I should prefer, however, to refer to it as the medical rather than the pathologic museum, because the latter term suggests a series of specimens in bottles, and the museum should be very much more than that.

The old museums were storehouses for pickled specimens, and such great collections as those of the German universities, the London hospitals and the Royal College of Surgeons in London and in Edinburgh played a great part in their day and still do so. But the modern tendency is to make things easier for the student, which can best be done by making them more interesting. This can be accomplished by presenting more than one aspect of a subject and by presenting the subject in as attractive a manner as possible. Those who visit the great Army Medical Museum at Washington will see both of these principles put into practice, and the scientific exhibits at the meetings of the American Medical Association are a striking demonstration of the drawing power of perfectly arranged displays.

I have had the experience of converting two of the classic forms of museum into something more modern in type, the one in Winnipeg, the other in Toronto. The basic principle underlying the work was the same in the two instances, but there was one difference worth noting. In Winnipeg the museum, as is commonly the case, consisted of one large room (although later a second was added), whereas in Toronto there was a large number of small rooms, one for the circulatory system, one for the nervous system, and so on. The convenience of the latter arrangement for teaching a number of groups is self evident.

The aim has been to make a clinicopathologic museum, a museum depicting disease in all its aspects. This is done by displaying, in addition to the gross specimens, illustrations of clinical conditions, microscopic appearances, roentgen ray findings, temperature charts, blood pictures, and so on. Nor is the historical side of medicine neglected. A few examples will illustrate the general idea. In the section on Addison's disease, in addition to the lesions of the adrenals there is a water color painting of a patient showing the characteristic bronzing of the skin, another of the pigmentation of the mouth and tongue, and a picture of Thomas Addison with a short biographic sketch. Exophthalmic goiter is illustrated by a picture of a patient with exophthalmos and enlarged neck, gross specimens of the thyroid, the microscopic picture and a representation of Robert Graves with biographic

Read before the joint meeting of the Council on Medical Education and Hospitals and the Federation of State Medical Boards of the United States at the Thirty-Seventh Annual Congress on Medical Education and Licensure, Chicago, Feb. 18, 1941.

notes. The section on glomerulonephritis is illustrated by a picture of Richard Bright, plates from Volhard and Fahr's classic monograph, a painting of the fundus showing albuminuric retinitis, and Oliver's reconstructions of the nephrons in chronic nephritis.

Instead of multiplying these examples endlessly, I will mention some details of the methods of display. One fundamental principle has been observed, namely that it is more restful to study a specimen when it is inclined than when it is upright. For this reason the ordinary museum display cases with horizontal shelves have been replaced by open stands of sloping shelves. There are five tiers of these shelves, and the whole fixture is painted white. The classic glass museum jars are not suitable for the narrow ledges which separate these shelves, but watch glasses of various sizes are admirably adapted to this purpose, as also are narrow glass cells which can be readily made by the technician. Both of these are much cheaper than the glass jar.

On the wall above the display stand there is a wooden board which serves to carry the various pictures. These illustrate the specimens on the shelves beneath. Attached to the lowest shelf there is a narrow box containing cards 7 by 8 inches in size. These are of sufficient size to contain a condensed copy of the catalogue description; indeed they replace the former catalogue. The back of the card can be used for a photomicrograph of the lesion, the whole being covered with bexoid and bound with fiber reinforcing tape. The advantage of this arrangement is that the student can sit down, study the specimen and read the description without having to move.

Pictures are of special value in the large room devoted to general pathology. Colored illustrations of the various fat, glycogen and amyloid stains recall to the student what he has seen or should see through the microscope. The inclusion bodies of virus diseases can be collected to form one composite picture. Another such picture shows the life cycle of the malaria parasite in man and in the mosquito, the anopheles mosquito compared with the culex, the temperature charts of tertian and quartan fever, the parasites in the brain and the pigment in the spleen. A third shows a map indicating the geographic distribution of trypanosomiasis, the trypanosomes in the blood, the tsetse fly, the lymphadenopathy and the native lying in his hut in the last stages of stupor. Colored illustrations of the rashes, mucous patches and condylomas of syphilis are surely as instructive as specimens of gumma and are absolutely necessary to complete the picture of the disease. There are hundreds of beautiful colored plates hidden away in atlases which remain unopened for years on library shelves. The best use to which an atlas can be put is to have its pictures torn out and displayed.

A feature of psychologic value is the use of the principle of what may be called paragraphing. In the bone room, for instance, the main disease groups such as osteomyelitis, tuberculosis and tumors are separated from one another by broad vertical strips of black cellophane. The individual members of such a group as bone tumors (osteogenic sarcoma, Ewing's tumor and others) are separated by thin green strips. The main groups are indicated by large labels on the wall, the subgroups by smaller labels at a lower level. This paragraphing not only makes it easy to find all the specimens of any given disease but enables the observer to carry away a visual memory of any particular group in which he may be interested.

In each of the small rooms a large viewing box is installed, which can be used for roentgenograms or transparencies of photomicrographs, clinical pictures or paintings of blood films. This box is deep enough to accommodate half a dozen wooden frames, each large enough to carry twelve 5 by 7 inch reductions; it is high enough so that all the frames can be pushed up out of sight above the limits of the glass. In the lung room one frame is devoted to tuberculosis, one to suppurative conditions, one to tumors, and so on. Whichever one is wanted is pulled down, so that the films are in front of the illuminated glass.

It will be evident that this type of museum is designed for the teaching not only of pathology but also of medicine and surgery, for it is a museum of disease and not merely of pathologic specimens. It is for the use not only of undergraduates but also of graduates and especially of those preparing themselves for the higher examinations. It is a museum of which it may be said that it is "a library composed, not of books, but of the things themselves about which books are written."

Medicine Antedates the Inception of Civil Law.—Medicine is the most ancient of professions, being older than Christianity and antedating the inception of civil law. It has its own system of rewards and punishments, its own disappointments and its own glories. It is a profession that has a broadening influence on the human mind and is characterized by a most splendid charity. It is an acquisition in the best tendencies and a protection against the worst tendencies. It retains for its profit no valuable discovery and it has no standing room for the quack, the scoundrel and the charlatan. Its best work is done in the light which beats upon its throne, not in the arena of politics encouraged by the cheers of thousands, not in the seclusion of the cloister sustained by the hope of eternal joy, but in the storm and wind swept country, in the streets of the village, in the boulevards of the city, on the desolate field of battle, where pain and pestilence, illness and misery are combated often with none but God to see it. It furnishes a curiously checkered life, a life in which storm clouds alternate with sunbeams. —Abell, Irvin: The Spirit of Medicine, *Pharos of Alpha Omega Alpha*, May 1941.

Digests and Reviews

TUBERCULOSIS AMONG STUDENTS AND GRADUATES OF MEDICINE

Abstract of an article by J. A. Myers, H. S. Diehl, Ruth E. Boynton, P. T. Y. Ch'iu, T. L. Streukens and Benedict Trach in the Annals of Internal Medicine, March 1941.

We have attempted to trace the 1,894 medical students who graduated or were scheduled to graduate from the University of Minnesota from 1919 to 1936 inclusive. Group 1 includes 1,441 students in the graduating classes from 1919 to 1932 inclusive, and group 2 includes 453 students in classes graduating from 1933 to 1936. Prior to 1929 no special routine examination for tuberculosis was made of students. Consequently information on group 1 was obtained largely through questionnaires. Information concerning 7.5 per cent of the entire group was not obtained.

GROUP 1

There were 1,304 replies from the members of the classes of 1919 to 1932. Forty-one (3.14 per cent) stated that clinical tuberculosis developed while they were in school. Ten others reported having had pleural effusions as students and 5 others that they had tuberculosis before entering medical school. Also 41 of the remaining 1,248 graduates (3.29 per cent), including 4 with pleural effusion, reported that tuberculosis developed in them after graduation from medical school. Thus, exclusive of the 5 who had tuberculosis before entering medical school 92 (7.07 per cent) have had the clinical disease while in school or since graduation. Of these, 11 (0.85 per cent) have died of tuberculosis.

Concerning tuberculin reactions, 389 have either had no tests or do not remember the results. Reactors to tuberculin varied from 15 to 33 until 1925, whereas the percentage of graduates who either had no tests or did not remember varied from 46 to 62 during this same period. In 1925 a tuberculosis service was made compulsory and in 1929 routine annual testing of all medical students was begun. The number reporting reactions has risen sharply since then, while the number who were not tested or do not remember has shown a sharp decrease. The 1932 class recorded 85 per cent reactors and only 3 per cent with no tests.

GROUP 2

The 453 students who entered the School of Medicine from 1929 to 1932 inclusive were carefully examined throughout their enrolment. The entire class entering in 1929 was tested with tuberculin and had annual roentgenograms of the chest regardless of the tuberculin reaction. The nonreactors on entrance were retested annually unless they became reactors. The members of the other three classes had tuberculin tests on entrance and annually or more often as long as they were nonreactors. Four of the 453 have died of nontuberculous diseases, leaving 449 students.

The percentage of reactors in these classes ranges from 33.3 to 37, while on graduation the percentage is from 57.7 to 77.9. The average in the four classes is 35.6 per cent on entrance, 41 per cent at the end of the third year and 67 per cent at the end of the fourth year, and 50.2 per cent of those who reacted negatively on entrance became positive before graduation. While there was an increase of reactors between entrance and the end of the junior year, the increase was greater during the senior year. Of the 449 students, 160 reacted to the test on entrance, 145 became reactors while in school and 144 were nonreactors on graduation.

Replies have been received from 369 of the 449 graduates. Of these 102 were from physicians who did not react to tuberculin at the end of the senior year. Sixty-five of these have had tuberculin tests since graduation, 30 of whom became reactors as interns, 15 following their internships and 20 are still nonreactors.

Although few of these graduates interned at hospitals requiring tuberculosis services, practically all were exposed to the unsuspected contagious case of tuberculosis admitted for some other coexisting condition. Moreover, most of these hospitals do not examine the members of their own personnel. To allow 46.2 per cent of uninfected interns to become infected during their hospital services constitutes a serious problem in tuberculosis control. From our observations among these physicians while they were students, together with their replies to our questionnaires, we now know of 350 (78.2 per cent) who react to tuberculin.

Students in the College of Education, the control group, came from the same general section of the country and while in school lived in the same general environment as the students of medicine except that they were not brought in direct contact with tuberculous patients as a part of their work. On entrance to the College of Education 24.8 per cent of the students reacted to tuberculin, while on graduation the percentage was 28.5. Thus, only slightly more than 1 per cent of the nonreactors became infected each year.

On entrance to the School of Medicine there were 160 students in the classes of 1933-1936 who had primary complexes as manifested by the tuberculin reaction. Five of these students are known to have since had diagnoses of clinical tuberculosis, a percentage of 3.1 as compared to 0.44, or 3 among 686 reactors from the Col-

lege of Education students. Of the 145 students in group 2 in whom the primary tuberculosis complex as manifested by the tuberculin reaction developed while in school, 14, or 9.6 per cent, have had lesions demonstrated as against the 3 among the College of Education students. However, 4 of the 14 had evidence only of primary foci located by roentgen study, 5 had only pleurisy with effusion, extrapulmonary clinical tuberculosis developed in 1, and clinical pulmonary disease developed in 4. The remaining 131 would not have known of the tuberculosis had it not been for the periodic tuberculin test.

Five of 45 students who replied to our questionnaire and stated that they had become tuberculin reactors since graduation have shown evidence of lesions on roentgen examination. Thus among the 305 students of medicine who were tuberculin reactors on entrance or who became reactors while in school, lesions which were located by roentgen or other methods of examination have developed in 18 as against the 3 in a total of 686 College of Education students who reacted to tuberculin either on entrance or subsequently. Neither in the School of Medicine nor in the College of Education do we know of any one in whom tuberculosis developed in the absence of a tuberculin reaction.

This study emphasizes, in addition to the hazards of exposure, the fact that the entire span of life must be considered in every case of tuberculosis whether the diagnosis is made by the tuberculin test alone or together with the demonstration of the location of lesions. In these students we have seen the evolution of tuberculosis: the history of exposure, the first tuberculin reaction, occasional location of the primary focus on roentgen examination and the reinfection type of lesions in the lungs. The procedure carried out in group 2 represents our future course in tuberculosis control.

PULMONARY TUBERCULOSIS IN MEDICAL STUDENTS

Abstract of an article by Richard G. Hahn, Carl Muschenheim and Jules Freund, published in the American Review of Tuberculosis, May 1941.

The present communication is a report of the results of tuberculosis case finding applied to groups of medical and nursing students at the Cornell University Medical College and the New York Hospital.

The methods employed were the intracutaneous tuberculin test and the roentgenographic examination of the chest. The reactions were read two days after the intracutaneous injections and were considered positive if the skin was raised over an area of a diameter of 5 mm. or more. The roentgenograms of the chest were made in the roentgen ray department of the hospital with standard technic, single posteroanterior views being used. Tests were made on first year medical students and student nurses within two months of admission to their respective schools and during the last month of their final year.

RESULTS WITH MEDICAL STUDENTS

Six first year classes were tested. The percentage of positive reactors varied from 75 to 89. Collectively, of the 315 first year students tested 259, or 82.2 per cent, were positive and 56, or 17.7 per cent, were negative. Fourth year classes graduating in 1935, 1936 and 1937 were similarly examined. Of the total of 147 tested 135, or 91.8 per cent, were found positive and 12, or 8.1 per cent, were negative. The incidence of positive reactors in the fourth year classes tested was thus 9.6 percentage points higher than in the first year classes. The percentage of negative reactors shortly before graduation in both the medical and nursing student groups has varied in different years from zero to 14.3. The average for the nursing student (of the classes of 1933 to 1939 inclusive) has been 6 per cent negative on graduation and, for the medical students, 8.7 per cent.

CHEST ROENTGENOGRAPHY

The medical students have had yearly roentgenograms of the chest since 1934. A total of 442 students each had at least one roentgenographic examination. Seventy-one, or 16.1 per cent, had calcified deposits in the tracheobronchial lymph nodes, in the pulmonary parenchyma or in both. These were interpreted as healed lesions of the childhood type. In 22, or 5 per cent, there were shadows at either or both of the extreme apexes of only several millimeters thickness. These were interpreted as thickening of the apical pleura with possibly some parenchymal involvement. This group was classified as doubtful. The calcified shadows and the doubtful apical shadows were found in every instance in the student's initial roentgenogram. None appeared in subsequent roentgenograms of those whose original film had been entirely negative. There was also no instance in which these shadows changed during the period of observation and, incidentally, no student whose initial film revealed either type of shadow was in the group in which defininite pulmonary infiltrations developed later. Five, or 1.1 per cent, had shadows characteristic of chronic pulmonary tuberculosis in the initial roentgenogram. The lesions were all minimal in extent. Only 2 of the 5 were found in the first academic year. The other 3 belonged to the classes of 1934 and 1935, which were not roentgenographed until their fourth and third years, respectively. Four other students, or 0.9 per cent, who had been negative in their initial

roentgenographic examination developed shadows characteristic of chronic pulmonary tuberculosis in subsequent years. Three were minimal and one was moderately advanced when found. None had complained of any symptoms before the lesion was discovered. In addition to having shown no roentgenographic evidence of tuberculosis, 3 of the 4 had originally been negative to 1 mg. of tuberculin. These 9 students, 2 per cent of the total, who were discovered to have chronic pulmonary tuberculosis, represent the entire number of cases found, including the apparently arrested as well as those in which progressive disease was demonstrated. Four of the 9 had lesions which were obviously progressive and these students were referred to sanatoriums immediately after discovery of the disease. The other 5, for various reasons not under our control, were allowed to continue at work and complete their course. Of these there were only 2 in regard to whom we possess subsequent information sufficient to determine whether their disease was arrested at the time of discovery. One of these has never had any symptoms or physical signs attributable to his lesion, which has remained unchanged in serial roentgenograms over a period of four years. The other is known to have had progression of his disease since graduation. The average age of all the students on entrance to the medical school was 22.

The tuberculosis rate in the medical students does not appear to be significantly above the expected rate in their age group. The rates both in the nursing and in the medical students are considerably below those reported in some other institutions of similar nature. Whether the relatively low incidence of pulmonary tuberculosis in the student groups is due entirely to rather rigid precautions is problematic. That the students are not completely protected from new infections, whether acquired within or without the hospital, is evident from the increase in the number of positive tuberculin reactors in successive years. Other factors which we think may contribute to the low rate of development of new lesions, at least in reference to the nursing students, are the conditions of housing and of nutrition which we believe to be exceptionally good, and the age of the students, who are somewhat older than in many other training schools. A high percentage of positive tuberculin reactors in our medical and nursing student groups on admission may indicate that most of them had a considerable degree of acquired resistance. Our experience would tend to support the observations of others that the students who are originally tuberculin negative are more likely to develop clinically significant disease than those originally tuberculin positive.

The incidence of pulmonary tuberculosis, inclusive of cases with arrested disease, was found to be 2 per cent for the medical students and 1.1 per cent for the nursing students. The incidence of new lesions developing after the initial roentgenographic examinations of entering students was 0.35 per hundred annually among medical students and 0.18 per hundred annually among nursing students.

It is our impression that asymptomatic tuberculosis in young adults eventually progresses in the majority of instances and should always be treated early. A definite policy, therefore, has recently been followed of recommending prompt treatment for all patients under 30 years of age in whom an infiltrative lesion has been discovered, regardless of the presence or absence of symptoms, the extent of the lesion or the results of sputum examinations and other laboratory procedures. We regard lesions presumed to be primary or first infection type as of as serious significance as those which appear to be the result of endogenous or exogenous reinfections.

Correspondence

SIGNERS OF THE DECLARATION OF INDEPENDENCE

To the Editor:—Dr. Ward called attention in the Student Section of THE JOURNAL, March 22, page 1331, to physician signers of the Declaration of Independence. However, the name of George Taylor, representing Pennsylvania, should not be included among them, as there is no evidence to this effect. The statement in the 1913 edition of Funk and Wagnall's "New Standard Dictionary" that he was a physician is apparently incorrect and was withdrawn from later editions. There is no mention of his being a physician in Kelly and Burrage's "American Medical Biographies," in F. R. Packard's "History of Medicine in the United States" or in the "Dictionary of American Biography" (Scribners, New York). In John Sanderson's "Biography of the Signers of the Declaration of Independence," to be sure, it is stated that Taylor commenced the study of medicine but soon became disgusted with it and, according to the Bucks County Historical Society publications, "ran away from home."

I quite agree with Dr. Ward that the medical profession should know more medical history, and I hope that he will agree with me that, as such history should be as accurate as possible, even this small point deserves correction.

E. B. KRUMBHAAR, M.D., Philadelphia.

DO YOU KNOW WHAT PHYSICIAN—

1. Discovered the parasite of malaria fever?
2. Became Poet Laureate of England?
3. Wrote "Rab and His Friends"?
4. Was the pioneer in the graphic study of cardiac arrhythmias?

DO YOU KNOW WHAT ANATOMIST

5. Painted what is considered to be the most famous portrait in the world?

DO YOU KNOW WHAT ZOOLOGIST

6. Discovered the cause of syphilis?

The answers are on page 2552.

Medical College News

Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items for consideration for publication in the Student Section.

Rush Medical College to Merge with Illinois

The board of trustees of Rush Medical College, Chicago, has asked the attorney general of the state to prepare a court petition for dissolution of the ties of Rush Medical College with the University of Chicago in preparation for a merger of its educational elements with the University of Illinois College of Medicine. The question is now before the circuit court. The newspapers reported, May 3, that these proposals are the result of long and extensive negotiations with the board of the Presbyterian Hospital and representatives of the medical and fiscal divisions of the two universities. Presbyterian Hospital is the teaching hospital for Rush Medical College, and members of its staff are all instructors at the college. The proposed plan is (1) severing of affiliation with the University of Chicago which has been continuous since 1924, and (2) abolition of Rush Medical College as an educational institution but retention of the Rush board to administer the physical properties of the college. Subdivisions of this main plan call for the absorption of all Rush medical instructors into the University of Illinois College of Medicine and affiliation of the Presbyterian Hospital with the state university's medical department. The Rush name will not be lost under the setup in that the Rush teachers will be known as Rush professors of the University of Illinois College of Medicine. The Rush buildings will be leased to the hospital for expansion purposes and possibly as instruction rooms for the medical students at Illinois. At this time there are about two hundred undergraduates in Rush Medical College in the junior and senior classes. The University of Chicago has agreed, according to the program, to graduate the junior class, but no more students will be accepted by Rush and the 1942 class will be its last. There will be no graduate school at Rush as once was planned. The Central Free Dispensary, which is operated in cooperation with Rush Medical College, will be taken over as an outpatient hospital consolidated with Presbyterian Hospital, with the hope that the dispensary and the hospital can have identical boards of trustees.

Loan Funds at Alabama

Students in the University of Alabama School of Medicine, University, maintain two loan funds, a fund for the purchase of library material pertaining to medical history, ethics and economics and a fund to provide a speaker each year in honor of Dr. William Crawford Gorgas. The Library Fund is known as the Freshman Memorial Library Fund and was established during the session of 1928-1929. Contributions are made voluntarily by practically all members of the freshman class. The librarian and the dean, ex officio, and two members of the faculty administer the fund. During the past decade more than six hundred volumes have been purchased, the *Annals of Medical History* subscribed for and portraits of James Marion Sims, John Y. Bassett and John Wyeth, all famous Alabama physicians, secured.

The James Marion Sims Loan Fund was spontaneously founded last year by voluntary subscriptions of the freshman class, varying in amounts from 50 cents to $35. The present freshman class has followed the procedure established last year. The professor of anatomy and the dean of the school, with a certified public accountant from the commerce faculty, have been named trustees of the fund.

The other loan fund in the medical school was established last year by the Sigma chapter of Phi Beta Pi Medical Fraternity. This fund is administered by a faculty committee of five with the dean as ex officio secretary and treasurer.

In addition, Alpha Epsilon Delta, premedical fraternity, sponsors an annual program in association with the medical school, and this society last year also established the Alpha Epsilon Delta Loan Fund with the chapter's faculty adviser, an associate professor of biology, and the dean of the medical school, ex officio, with the same professor of accounting from the School of Commerce as the third member. All three funds are audited by a certified public accountant annually and reports made to the donors.

The Gorgas Medical Society consists of all students in good standing enrolled in the school after the first semester. All members of the society and members of the faculty contribute $1 each with which a speaker is secured annually in honor of the birthday of Dr. William Crawford Gorgas of Alabama. This year Prof. Anton J. Carlson of Chicago will be the speaker. The Gorgas Medical Society in the school chooses annually a limited number of the sophomore class as Gorgas fellows. This is the highest honor awarded during the session.

Oklahoma Seniors Apply for Commissions

Twenty members of the senior class of the University of Oklahoma School of Medicine, Oklahoma City, have applied for commissions in the Medical Reserve Corps of the U. S. Army. The commissions are being granted by the War Department, our correspondent states, with the understanding that these young physicians will not be called into actual military service until after completing one year's internship following graduation.

A plaque in honor of the late Dr. Leroy Long, dean of the University of Oklahoma School of Medicine for many years, was dedicated by appropriate ceremonies in the auditorium of the school May 19. The plaque

was erected by the Oklahoma State Medical Association and the alumni association of the medical school and was modeled by Joseph R. Taylor, associate professor of art at the university.

Pennsylvania's Annual Undergraduate Meeting

At the thirty-third annual meeting of the Undergraduate Medical Association of the University of Pennsylvania, the opening address, by Dr. John H. Stokes, was "The Young Doctor and the War." Dr. Cornelius P. Rhoads, New York, of the Rockefeller Institute for Medical Research and director of the Memorial Hospital for the Treatment of Cancer, spoke on "Chemical Aspects of Cancer," and A. Baird Hastings, Ph.D., Hamilton Kuhn professor of biological chemistry, Harvard University, Cambridge, Mass., on "The Case for the Intracellular Fluid." Papers on research were presented by nine students. The May Ellis Bell Prize was presented to Christian J. Lambertsen '43 for his paper on "A Diving Apparatus for Life Saving." The John G. Clark Prize was awarded to John C. Lilly '42 for his paper on "The Electrical Capacitance Diaphragm Manometer: A New Apparatus for Direct Blood Pressure Determination." The Grahye Simpson Priestley Prize was awarded to Martin G. Netsky '43 for his paper "Some Effects of Desoxycorticosterone and Related Compounds on the Mammalian Red Cell." Miss Lillian B. Panzer '44 was given honorable mention for her paper on "Experimental Hypoprothrombinemia."

California's Gold Headed Cane

At the annual gold headed cane ceremony at the University of California Medical School, San Francisco, April 14, Robert H. Crede, a senior student, received the award. The guest speaker on this occasion was Dr. George Blumer, professor of medicine at Yale University School of Medicine, New Haven, Conn., who also was awarded a gold headed cane. A cane is given annually to the member of the senior class who is adjudged most likely in the opinion of his classmates and the faculty to be eminently successful in the profession. This ceremony is adopted from an old English custom in which a single gold headed cane was handed down through generations of eminent British physicians.

New Indiana A. O. A. Members

The following upper classmen at Indiana University School of Medicine, Bloomington, have recently been elected members of A. O. A. honorary scholastic society: Wallace E. Bash, Warsaw; Margaret Ann Bassett, Thorntown; Mary H. Beall, Rushville; Otis R. Bowen, Crown Point; Lawrence A. Cantow, New York; Jack Dick, Huntington; Laura Hare, Indianapolis; Edgar A. Hawk, New Palestine; John E. Heubi, Jeffersonville; Joe Humphreys, Cloverdale; Joe H. Jewett, Carmel; William W. Krieble, Terre Haute; Griffith Marr, Columbus; Charles F. Martin Jr., Logansport; Sherman Minton Jr., New Albany; Theodore F. Schlaegel Jr., Indianapolis, Lawson F. Smith, Indianapolis, and James B. Warriner, Indianapolis.

Harvard Awards Christian Prize

John William Raker, a fourth year student, has been awarded the Henry A. Christian prize at the Harvard Medical School, Boston, which is given to a student in the senior class "who has displayed diligence and notable scholarship and offers promise for the future." Mr. Raker, who is from Kutztown, Pa., graduated from Bucknell University in 1937. The award was established a few years ago in honor of Dr. Henry A. Christian, professor of theory and practice of physic, emeritus.

Dr. Brücke Goes to East Indies

The fourth year students at the University of California Medical School, San Francisco, were recently addressed by Dr. Ernst T. von Brücke, of the physiology department of Harvard Medical School, Boston, who was en route to the Dutch East Indies, where he will engage in surgical work for the Dutch army. Dr. Brücke lectured on his surgical experiences with a Red Cross unit sent by the Netherlands to Ethiopia a few years ago and recently to Finland.

Among the seminars conducted recently at the medical school on the early medical history of California was one conducted by Dr. John B. de C. M. Saunders on "Chacon Daza, Author of the Earliest Textbook of Surgery on the North American Continent."

The Contin Society

Dr. Arthur Fishberg delivered the first annual lecture of the Contin Society, an honorary organization at the New York Medical College and Fifth Avenue Hospitals, New York, May 9, on "Recent Developments in Essential Hypertension." Dr. Samuel J. Kopetzky, chief of the medical division of Selective Service of the City of New York, addressed the annual induction meeting of the Contin Society, February 6, on the draft in relation to doctors, interns and medical students. The following students were inducted into the society: seniors—Milton Willner, Sidney Cramer and A. Winifred Phillips; juniors—Letizia Ciaramelli, Theodore Struhl, Thomas Benson and Abraham Umansky. The faculty members elected to honorary membership to this society were Dr. J. A. Werner Hetrick, acting dean and head of the department of otolaryngology; Dr. Reuel A. Benson, head of the department of pediatrics, and Dr. Milton J. Raisbeck, associate professor of medicine.

University of California Charter Day Exercises

Students, faculty and alumni attended Charter Day exercises held in San Francisco, March 28-29, at the University of California Medical Center to celebrate the university's seventy-third birthday. The dean of Stanford University School of Medicine, Dr. Loren R. Chandler, spoke on "The Future of the Student and Recent Graduate." The celebration included clinics, demonstrations at the medical school, the annual meeting and the banquet of the medical alumni, at which Dr. Karl F. Meyer, professor of bacteriology, discussed "The Relationship of Public Health to National Defense."

Undergraduate Meeting at George Washington University

One day in the year is set aside for an undergraduate medical meeting at the George Washington University School of Medicine, Washington, D. C.; the second annual meeting of this kind was held at the medical school April 19. The morning of that day was devoted to the presentation of seventeen papers by students who have been engaged in research. In the afternoon the student body was addressed by Dr. Nicholson J. Eastman, professor of obstetrics, Johns Hopkins University School of Medicine, Baltimore, on "Asphyxia Neonatorum." In the evening the first annual medical ball was held at the Shoreham Hotel.

Medical History at Long Island

A group of students at Long Island College of Medicine, Brooklyn, have formed a medical history club under the tentative name of Donellon House Club. At the first meeting, February 26, among other subjects

presented was "Semmelweis and Puerperal Sepsis" and "Medicine in Old London." At the second meeting, April 17, Jean A. Curran, dean of the medical school, presented a paper entitled "An Unknown Genius of American Medicine" (John Shaw Billings).

New Yale Members of A. O. A.

The Yale chapter of Alpha Omega Alpha, medical honorary society, announced on May 15 the election of the following medical students to membership in the society: Gioacchino S. Parrella, New Haven; Irving Waltman, Hartford; James M. Bunce, Hartford; Allan V. N. Goodyer, Stamford; John R. Lincoln, West Hartford; Maurice Tulin, Hartford; Antonio J. Waring Jr., Savannah, Ga., and Irving N. Wolfson, New York. Dr. Arnold L. Gesell, director of the Clinic of Child Development of Yale University, was elected an honorary member. Following the banquet and initiation, which was held in the Yale Faculty Club, Rudolf Schoenheimer, associate professor of biochemistry at Columbia University, New York, gave the annual Alpha Omega Alpha lecture on "The State of the Structural Elements of Life."

Premedical Fraternity at Detroit

The national honorary premedical fraternity, Alpha Epsilon Delta, installed its thirty-second chapter at the University of Detroit, Michigan, March 8, 1941, when the Iota chapter of Omega Beta Pi became the Michigan Alpha chapter of Alpha Epsilon Delta with the induction into the fraternity of twenty students and two faculty members.

Woman's Medical College

The third and fourth year students of Woman's Medical College of Pennsylvania, Philadelphia, were addressed, January 2, by Dr. Bertha Van Hoosen, of Chicago, on "Surgery Made Plain." The lecture forum of the college presented a symposium on "Chronic Cumulative Lead Intoxication," February 14; the speakers were Dr. Helena E. Riggs and Messrs. Feodor Letonoff and John Reinholt.

The Marion Sims Society

The first of a series of annual lectures, sponsored by the Marion Sims Clinical Society of the Medical College of the State of South Carolina, was given at the college at Charleston, April 25, by Dr. James H. Gibbes of Columbia, S. C., whose subject was "Marion Sims, Physician and Man." Dr. Gibbes was introduced by Dr. Robert Wilson, dean of the medical college. The lecture was attended by the students, members of the faculty and other physicians of the community.

College of Medical Evangelists

Dr. Oswald S. Lowsley, New York, addressed the junior and senior classes at the College of Medical Evangelists, Los Angeles, February 12. On this occasion a moving picture on venereal diseases was shown. ——Dr. Emanuel Libman, New York, conducted a clinic for the junior and senior students, February 7, at which time two patients with Libman-Sachs' disease were presented.

Annual Nu Sigma Nu Lecture at Colorado

The third annual Nu Sigma Nu Lecture at the University of Colorado School of Medicine was given April 21 by Bradley M. Patten, Ph.D., head of the department of anatomy at the University of Michigan Medical School, Ann Harbor, on "Micro-Moving Pictures of the Early Development of the Cardiovascular System in Living Embryos." Dr. and Mrs. Patten and several faculty members were dinner guests at the Nu Sigma Nu House before the lecture, and open house was held later in the evening.

Haggard Memorial Lecture at Vanderbilt

The Alpha Kappa Kappa fraternity at Vanderbilt University School of Medicine, Nashville, Tenn., has established an annual lectureship in memory of the late Dr. William D. Haggard, professor of surgery and clinical surgery at the school for many years before his death, Jan. 28, 1940. The first lecture was delivered on January 17 by Dr. Mont R. Reid, Christian R. Holmes professor of surgery at the University of Cincinnati College of Medicine, on "Experiences in Vascular Surgery."

"DO YOU KNOW"

Following are answers to the questions appearing on page 2550:

1. Alphonse Laveran (1845-1922) of Paris made this discovery, Nov. 6, 1880, while an army surgeon in Algeria. Dr. Laveran was awarded the Nobel prize in 1907.

2. Dr. Robert Seymour Bridges (1844-1930), the only physician to hold this position. Dr. Bridges studied at St. Bartholomew's Hospital, London, and held several hospital appointments in that city before withdrawing from the active practice of medicine at the age of 37. His last work, "The Testament of Beauty," was published in 1929.

3. Dr. John Brown (1810-1882) of Edinburgh, the pupil and later assistant of the famous Syme.

4. Sir James Mackenzie (1853-1925), a graduate of Edinburgh, first made simultaneous records of the arterial and venous pulses to elucidate the clinical condition of the heart. He practiced nearly thirty years in a small city, then went to London as consultant in 1907 and, according to Garrison, made his mark by his sincere, earnest attitude toward the sick and his sterling books on the pulse and heart disease, including angina pectoris. He retired from practice in 1918 and the next year started the Institute for Clinical Research at St. Andrews. Garrison considers Sir James one of the greatest modern bedside physicians; he attracted patients from all over the world. By a strange irony of fate, he died of angina pectoris, a disease of which at that time he probably knew more than any one else.

5. Leonardo Da Vinci (1452-1519), who was the first to describe hardening of the arteries. He originated the idea of studying anatomy for the purpose of improving art. His anatomic drawings made from actual dissections were so accurate that many of them could be used in textbooks of anatomy today. He was born in the village of Vinci, near Florence, Italy, and was placed in the studio at an early age, where he served many years as an apprentice of painting. His most famous portrait, Mona Lisa, was of the young wife of a rich old man, Francesco del Gioconda.

6. Fritz Schaudinn (1871-1906) in May 1905, while working with Erich Hoffmann. Schaudinn took his doctor's degree in zoology in Berlin in 1894 and in 1906 he became director of protozoology at the Institut für Schiffs- und Trophenhygiene at Hamburg. He was the son of an East Prussian innkeeper.

UNTIL SEPTEMBER

The Student Section will not be published during June, July and August. In the meantime, papers, news and other items for the autumn issues of this section may be submitted.

Book Notices

Temperature: Its Measurement and Control in Science and Industry. Papers Presented at a Symposium Held in New York City, November 1939, Under the Auspices of the American Institute of Physics with the Cooperation of National Bureau of Standards, National Research Council and Officers and Committees of American Ceramic Society et al. Cloth. Price, $11. Pp. 1,362, with illustrations. New York: Reinhold Publishing Corporation, 1941.

This is an authoritative, well documented, extensive survey of the whole field of temperature. Of the twelve hundred and ninety-two pages of text, some two hundred and fifty are directly concerned with temperature and its regulation in man and temperature in biology. The rest of the book is concerned with the concept of temperature in the various natural sciences and in industry with quite complete discussions of theoretical points, as well as practical applications and new methods and apparatus. There are thirteen chapters, each made up of from six to fourteen papers by recognized authorities in the field, as well as an extensive appendix and an excellent author and subject index. Most papers presented have a complete bibliography up to November 1939, and there are also frequently included discussions of the paper by other authorities. The section on temperature in biology discusses such questions as the temperature limits of life, the development of homeothermy in animals, temperature factors in production and the normal and febrile temperature pattern of laboratory animals. The section on temperature and its regulation in man considers among other things the temperature sense, heat exchanges under normal and abnormal conditions, thermoregulatory mechanisms and their disturbance, standard operative temperatures and some of the earlier observations on reduced temperature therapy. The book as a whole is technical yet interesting reading. It should be an invaluable handbook for reference by any one interested in the subject of temperature, though the clinical implications and control of abnormal temperatures are not as fully dealt with as one might wish.

A Yankee Doctor in Paradise. By S. M. Lambert, M.D. Cloth. Price, $3. Pp. 393, with portrait. Boston: Little, Brown & Company, 1941.

For twenty years Dr. S. M. Lambert was stationed in the South Seas working for the Rockefeller Foundation. To him particularly was assigned the control of hookworm. It became necessary that he determine the extent to which natives in all portions of the South Seas were infected with this parasite and also to apply the technics that have been developed by scientists for the treatment of such infection. As a physician and sanitarian he did not limit himself exclusively to hookworm but became familiar with other conditions that are prevalent, including particularly leprosy, tropical sores and the venereal diseases. This book, however, is no dryasdust recapitulation of the epidemiology of the South Seas. It is more fascinating by far than any novels of the current season. It is devoted equally to the anthropology and to the ethnology of the native tribes. He relates with a sharp sense of humor innumerable incidents which add excitement to the life of a physician who serves among primitive peoples.

THE JOURNAL of Nov. 19, 1921 contained an article by Maurice C. Hall on the use of carbon tetrachloride in the removal of hookworm which was the answer to the problem of the control of hookworm, and the arrival of that issue in February 1922 in the South Sea Islands was the inspiration for the tremendous success which Dr. Lambert achieved in his work.

In this fascinating book is told the story of the 325 pound queen of Tonga. Here is revealed the development of pidgin English and the manner of its use in the promotion of modern health and hygiene. Here is the inside story of a health ambassador working with amazing success to preserve the lives of the Fijian race and attempting to bring to it the blessings of civilized man without the inevitable destruction that seems to be associated with the work of civilized man in the tropics. Here is a book which might well be read by every medical student to prove to him that the advancement of scientific medicine has not destroyed the inspiration and romance of medical service. No doubt, one of the most important of Dr. Lambert's accomplishments was the establishing of a school for the teaching of natives, who will themselves endeavor to aid in the stamping out of the diseases which are destroying them. Today Dr. Lambert and his devoted wife have retired to a well earned rest in California, but for him and for every reader of his book Fiji becomes instantly alive and beckons.

Physikalisch-diätetische Therapie nach klinischen Gesichtspunkten. Von Dr. Hans-Georg Scholtz, dirigierender Arzt der Abteilung für physikalische Therapie am Städtischen Rudolf-Virchows-Krankenhaus, Berlin. Paper. Price, 15 marks. Pp. 303, with 93 illustrations. Leipzig: Georg Thieme, 1940.

This textbook is divided into two main sections. The first section deals with the technic of application, the physiologic effects of physical agents and the fundamentals and administration of therapeutic diets. In the second section the clinical application of physical and dietetic therapy is considered.

The text is a peculiar hodgepodge of good and poor methods of treatment, hydrotherapy, colonic irrigation, thermotherapy, balneology, the use of various types of packs and compresses, light therapy, electrotherapy, including galvanic and faradic therapy and the employment of high frequency currents, mechanotherapy, including massage and manipulation, and the technic of local blood letting and Bier's passive hyperemia. In the part on dietetics, the author includes a discussion of the principles of nutrition, stipulations for the administration of therapeutic diets and indications for their employment in various diseases.

The text is well illustrated, but here again there seems to be little discrimination between what is good and what is bad in the field of physical and dietetic therapy. Whereas there are excellent illustrations on corrective exercises and underwater gymnastics, on the other hand there are many illustrations of antiquated devices such as the Schnee bath, queer and antiquated methods for applying colonic irrigations, electric baths and descriptions of such comparatively useless procedures as sand baths, all interspersed with excellent illustrations of the more modern methods of applying massage, heat, exercise and electrotherapy.

The part on dietetics seems to be subordinated to the section on physical therapy; it probably would have been best if this phase of the subject had been dealt with in a separate book.

In the clinical section of the book the employment of physical agents and diets is considered in connection with the treatment of certain infections, circulatory, respiratory and rheumatic diseases, as well as in diseases of the gastrointestinal, genitourinary and nervous systems and disease of constitutional and metabolic origin. Although there is much of interest in this section, there is also the usual lack of discrimination concerning proper indications. The illustrations are numerous and good. There is an adequate subject index, but no bibliography or list of references is appended. The book is recommended to any one who is interested in this field of therapy and who is capable of discriminating between the suitable and unsuitable material presented in the text. It is not recommended for the beginner in this field of therapy.

Treatment in General Practice: Surgery (Continued). Volume IV. Articles Republished from the British Medical Journal. Cloth. Price, 16s. Pp. 562, with 143 illustrations. London: H. K. Lewis & Co., Ltd., 1940.

This volume is a satisfactory presentation of the treatment of many common surgical conditions encountered in peacetime practice, handled by the general practitioner. It is satisfactory because facts of practical importance are stressed in an authoritative way by adhering to well tested principles and, for the most part, to sound, accepted methods of treatment. None of the articles are long, controversial or concerned with obscure conditions. It is a tribute to the editing that there should be such uniformity in concise presentation of significant material on so many subjects by so many authors. Each chapter is introduced by sufficient description to make identification of the lesions possible, usually assisted by plain but adequate illustrations (although some of the photographic cuts are poor). This is important because not a few of the relatively common but disabling injuries with the treatment of which a general practitioner is frequently confronted (such, for example, as hand infections and injuries about the shoulder joint) are often not correctly diagnosed or properly treated.

The material covered includes common traumatic injuries of the extremities, chest and spine and their associated complications, frequently encountered disturbances of the genitourinary tract (urinary retention, phimosis, hydrocele), rectal lesions (hemorrhoids, prolapse, pruritus), common infections, simple amputations, the treatment of varicose veins and of the complications of varicose veins, and the prevention and treatment of bed sores and essential principles so far evolved in the use of the newer chemotherapeutic agents as applied to surgical disorders.

No effort has been made in any of the volumes of this series to deal specifically with the injuries of modern warfare. Much that the book says regarding trauma is applicable to the treatment of these conditions, but no special technics which apply to the handling of such injuries and no injuries peculiar to the present military situation are described. Any one interested primarily in the latter must look elsewhere, and for this reason the book may be undeservedly neglected. In spite of the unusual interest in military surgery at the moment, the book should be popular both in England and here: the points of view are essentially the same, the ground is well covered and the essence of each subject, because of the way it has been presented, is quickly and easily grasped.

A Method of Anatomy: Descriptive and Deductive. By J. C. Boileau Grant, M.C., M.D., Ch.B., Professor of Anatomy in the University of Toronto. Second edition. Cloth. Price, $6. Pp. 794, with 651 illustrations. Baltimore: William Wood & Company, 1940.

In the teaching of anatomy there is no substitute for actual dissection of the human body. However, anatomy books form an invaluable aid to the acquisition and retention of anatomic details. The various textbooks of anatomy have grown up traditionally with the development of the science of human anatomy and therefore represent careful analytic description and discussion revised again and again as they have been put to use and found wanting. The fact that anatomy is occupying less space in the student's curriculum necessitates a brief but thorough and more functional approach. That is the aim of this textbook. Its success can be appreciated only from experience. In many ways it should appeal to students who find existing textbooks replete with exhaustive and fatiguing detail. It resorts to simple uncolored drawings, usually schematic, which are easy to follow. It lacks the superb anatomic drawings of the better known anatomic works, and as a source of ready reference for review it cannot compare with the older style books. While it may prove of value in the teaching of anatomy, the student is less likely to treasure it and refer to it as he does the more exhaustive volumes. Students who use this book will be pleased by its refreshing attack on a difficult subject. Whether it can replace the well established, traditional textbooks is questionable.

Health of White Settlers in Surinam. By N. H. Swellengrebel, Professor of Parasitology, University of Amsterdam, Amsterdam, in collaboration with E. van der Kuyp, Government Physician Paramaribo. Colonial Institute at Amsterdam, Special Publication No. LIV. Department of Tropical Hygiene No. 16. Paper. Pp. 118, with 7 illustrations. Amsterdam: The Institute, 1940.

The International Refugee Colonization Society was founded in the Hague to finance the wholesale emigration of Jews and other refugees and to ascertain which countries would offer the best opportunities for settlement. From the first the organization was interested in Surinam in spite of its bad repute and the numerous failures at European colonization. Most of the work of the commission sent to Surinam was interrupted by the war, but the sanitary phases are preserved in this report.

The main portion of the report is divided into five sections as follows: general information, which includes a brief account of the climate, soil, population and governmental districts; sanitary conditions in Surinam, which summarizes and discusses the significance of the vital statistics of the area; sanitary history of the white settlement in Surinam; malaria in rural Surinam, and the prevention of diseases in a future settlement.

Professor Swellengrebel's scholarly and critical examination of the health conditions brings out some surprising conclusions. The health conditions on the coast of Surinam are unbelievably good for a tropical area. They are exceptional in the tropical town of Paramaribo. In the rural areas malaria and hookworm lead all other diseases in importance, and the history of the attempts of white settlement in Surinam suggest that most failed because of malaria. In spite of these diseases, however, the average rural death rates are lower than in Paramaribo. The Bush Negroes are a serious reservoir of malignant tertian malaria for colonists, as they harbor large numbers of the parasite without marked inconvenience. In general, health conditions offer no obstacle to the settlement of Surinam with white persons provided the colonists avoid certain highly malarious areas (in particular the interior in or near the bush) and do not wantonly neglect certain elementary laws of health. Throughout his discussion the author, in common with certain other modern historians, warns against ascribing too great an importance to unfavorable health conditions as compared to economic factors in limiting colonization with white persons. The present volume is recommended as an exceptionally interesting and valuable contribution to tropical medicine.

Anatomy and Physiology Laboratory Guide. By Edmond J. Farris, Executive Director, Associate in Anatomy, The Wistar Institute of Anatomy and Biology, Philadelphia. Third edition. Paper. Price, $1.60. Pp. 144, with 126 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1941.

While the reviewer is not familiar with earlier editions of this manual, it is obviously designed for a school of nursing. As such it appears to be admirably developed. According to the preface, some valuable improvements have been made. The general plan is one of integration of anatomy with physiology. For example, unit 1 is devoted to the body as an integrated whole, and in this is an introduction to anatomy together with some simpler physiologic experiments. Unit 2 deals with the erect and moving body and is similarly integrated. The illustrations include line diagrams, schematic diagrams, drawings and structures that the student must identify by labeling a roentgenogram of an erect human subject, colored schematic drawings of muscles, reproductions of simpler kymographic tracings and three full pages of photographs of laboratory equipment with sentence descriptions of each. There is also a table of more than forty teaching films, listed by unit, together with commercial distributors. This includes all the best sources of this type of teaching material. The manual contains a surprising amount of information for the purpose for which it is designed.

Diagnosis and Treatment of Arthritis and Allied Disorders. By H. M. Margolis, M.D., M.S., F.A.C.P., Chief, Arthritis Service, St. Margaret Memorial Hospital, Pittsburgh. Cloth. Price, $7.50. Pp. 551, with 140 illustrations. New York & London: Paul B. Hoeber, Inc., 1941.

This book was written to indicate to the family physician the possibilities of preventing and treating arthritis and its allied disorders. The author emphasizes the purely clinical aspects of the treatment and simple office procedures. The introduction is well written. The illustrations of the constitutional basis on which atrophic arthritis is built, using the pyramid as an example, are instructive. The chapter on the pathologic changes is a little short. The author presents a fair and just account of the importance of focal infection in atrophic arthritis. In the illustration on head traction, the author has not shown the raising of the head of the bed. His discussions of the cervical rib and the scalenus anticus syndrome are well worth the time required to read them. One of the most valuable parts of the book is the author's fifteen section discussion of low back and sciatic pain. His choice of borrowed illustrations is good. The bibliography is up to date. On the whole this is a good book and is well worth reading.

Allgemeine Elektrokardiographie. Von Professor Dr. Eberhard Koch, Direktor des Physiologischen Universitäts-Institutes Giessen. Mit einem Anhang: Richtlinien für die Auswertung eines Ekg. Von Dr. Elsbeth Koch-Momm. Fifth edition. Paper. Price, 2.25 marks. Pp. 49, with 44 illustrations. Dresden & Leipzig: Theodor Steinkopff, 1940.

The new edition is a slight amplification and revision of the previous edition of this short monograph. It is useful in introducing the reader to the theoretical aspects of electrocardiography. It can be recommended to those seeking such information.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

CLIMATE AND ARTHRITIS

To the Editor:—Would you please advise us regarding arthritis in North and South Dakota? We are interested in the prevalence in North and South Dakota, as well as whether a patient is benefited or harmed by residence in that state. We understand the ambiguity of the latter statement but would appreciate any information you may give us along these lines.

Percy A. Ward, M.D.
John T. Pewtors, M.D.,
Minneapolis.

ANSWER.—There are available no comprehensive figures on the incidence of rheumatic diseases in North or South Dakota. The recent (1935-1936) National Health Survey gave the national incidence of arthritis and rheumatism but not the incidence by states. Perhaps unpublished data thereon could be obtained from the United States Public Health Service, which conducted the survey. The incidence of rheumatic disease is reputedly considerably greater in the Northern than in the Southern states. For example, rheumatic fever is several times more common about latitude 47 north, that of North Dakota, than it is in latitude 25 north, that of Florida (Seegal, David; Seegal, Emily B. C., and Jost, Elizabeth L.: A Comparative Study of the Geographic Distribution of Rheumatic Fever, Scarlet Fever and Acute Glomerulonephritis in North America, *Am. J. M. Sc.* **190**:383 [Sept.] 1935. Nichol, E. F.: Geographic Distribution of Rheumatic Fever and Rheumatic Heart Disease in the United States, *J. Lab. & Clin. Med.* **21**:588 [March] 1936). For the size of their populations there is probably more chronic arthritis in the Dakotas than in the Southern states. The inquirer, however, is obviously concerned not with the possible appearance of arthritis among nonarthritic persons who move to the Dakotas but with the probable influence of the climate on an already existing arthritis. It is not stated what kind of "arthritis" the patient has. Gouty and osteoarthritis (hypertrophic) are affected by weather less notably than is rheumatoid arthritis. Patients who have the latter disease generally feel worse in cold weather and in winter, better in warm weather and in summer; they often can predict the approach of a storm by an alteration in their symptoms. But there are so many exceptions to these generalizations that the effect of climate and weather on arthritic patients has never been precisely defined.

Climate and weather are a composite of temperature, humidity, barometric pressure, atmospheric electricity and other factors. Rentschler, Vanzant and Rowntree (Arthritic Pain in Relation to Changes in Weather, THE JOURNAL, June 15, 1929, p. 1995) noted that barometric pressure influenced the symptoms of most arthritic patients more consistently than did temperature or humidity. But it did not influence all arthritic patients in the same way; some felt better when the barometer rose, others felt better when the barometer fell. Humidity has a definite part in determining an arthritic patient's symptoms. The arthritic feel better on cold dry days than on cold damp days; also they feel better on hot dry days, but on hot humid days they may feel worse even than in winter time (Coste, F., and Forestier, J.: Rheumatic Meteoropathology, *M. Press* **197**:116 (Aug. 10) 1938). And despite the notable shifts in temperature which occur between the winter days and the nights in Arizona, arthritic patients generally feel better there because of the stability of the other factors that may affect them adversely.

A recent survey led Tegner (Treatment of the Rheumatic Diseases in the United States and the Continent of Europe, *Ann. Rheumat. Dis.* **1**:249 [Oct.] 1939) to conclude that in the temperate zone local climate is a relatively unimportant factor in the incidence of chronic rheumatism, although it may be a factor in aggravating the symptoms of the disease. Of greater importance than the general climate is "the microclimate" of home and working place (Hill, Leonard: Rheumatism and Climate, *Brit. M. J.* **2**:276 [Aug. 5] 1939). According to Hill, cold, damp, atmospheric electricity and cyclonic disturbances are not important. Eskimos and Lapps have much less rheumatism than dwellers in temperate zones who live indoors in badly ventilated, artificially heated houses. Despite the cold, none of Scott's or Shackleton's arctic explorers had rheumatism.

The winters of the Dakotas are cold, but so are those of Minnesota, and it is probable that an arthritic person from Minneapolis would find no notable alteration in symptoms after moving to the Dakotas. Patients in these states would feel more comfortable were they able to avoid the rigors of the Northern winters. But to combat the latter much can be done in the way of warm, well ventilated houses, the use of warm but porous clothing, and the consistent daily use of various simple home methods of physical therapy supplemented by professional physical therapy and other remedies. Such is the nature of chronic rheumatoid arthritis that many a victim of that disease may be much better off in the Dakotas if he carries out a careful schedule of orthodox antiarthritic therapy than if he treks south to lie neglected in the sun without benefit of other treatments.

EFFECTS OF ORALLY ADMINISTERED ALUMINUM ACETATE SOLUTION

To the Editor:—Is aluminum in the form of liquor alumini acetatis ingested orally absorbed into the general circulation? Or is practically 100 per cent of it eliminated by the bowel? If absorbed does it affect the circulation, glands or other soft tissues or the bone? Is there any contraindication for its ingestion orally other than its slight astringent effect?

A. C. Howe, M.D., Brooklyn, New York.

ANSWER.—The soluble salts of aluminum, like those of other heavy metals precipitate proteins, are astringent and are only slightly absorbed if at all. Some of the early investigators reported that the soluble aluminum compounds are completely (within the limits of experimental error) eliminated in the feces. Other investigators have shown that there is slow absorption of small quantities of aluminum compounds when taken orally. These small amounts are rapidly eliminated in the urine with no storage of aluminum in the tissues of the body. Symptoms of aluminum poisoning due to storage of aluminum in the tissues of the body do not occur when aluminum salts are given by mouth, even in large doses and over long periods. The metal is excreted in the feces partly as phosphate, thus deflecting the phosphates from the urine or preventing their absorption and utilization. Unless the income of phosphorus is deficient, this is practically unimportant. Rickets has been produced in animals by continued overdosage with aluminum salts. Because they are not readily absorbed, even large doses cause only local exudative inflammation of the alimentary canal. The astringency of aluminum compounds tends to produce mild to severe constipation which may be controlled by the administration of liquid petrolatum.

Solution of aluminum acetate (Burow's solution) of the National Formulary VI contains about 5 per cent of neutral aluminum acetate and, as it is prepared from lead acetate and aluminum sulfate, it may contain a small amount of lead as an impurity. Solution of aluminum subacetate of the National Formulary VI contains about 8 per cent of aluminum subacetate (equivalent to about 10 per cent aluminum acetate) and is identical to the solution of aluminum acetate (Burow's solution) described in the British Pharmaceutical Codex, except that the latter contains approximately 17.8 per cent of aluminum subacetate (equivalent to approximately 22.5 per cent of aluminum acetate). Neither of the National Formulary preparations is recognized for internal use, and the solution of aluminum acetate (N. F.) would be undesirable for such use because of the danger of poisoning from the lead impurity. It should be noted that while the synonym Burow's solution is applied in both instances to the names solution of aluminum acetate, these solutions are described differently in the National Formulary and the British Pharmaceutical Codex, only the former containing lead as an impurity. The similarity of the latter with that of the official subacetate solution is illustrated as follows:

Solution of Aluminum Subacetate (N. F.)		Solution of Aluminum Acetate (B. P. C.)	
Aluminum sulfate	160 Gm.	Aluminum sulfate	225 Gm.
Acetic acid	160 cc.	Acetic acid	250 cc.
Precipitated calcium carbonate	70 Gm.	Calcium carbonate	100 Gm.
Water, a sufficient quantity to make	1,000 cc.	Distilled water	750 cc.

Recently A. J. Helfet (A New Conception of Parathyroid Function and Its Clinical Application, *Brit. J. Surg.* **27**:651 [April] 1940) has reported the use of a solution of aluminum acetate in the treatment of parathyroid diseases. Based on the theory that retention of phosphate acts as a stimulus to increased secretion of parathyroid and that this results in a "compensatory" hyperparathyroidism with essentially normal glands and blood calcium and phosphorus values, this investigator has proposed the oral use of aluminum acetate for the removal of phosphate from the body in the treatment of secondary hyperparathyroidism

or generalized fibrocystic disease (not due to adenomatous parathyroid glands), rheumatoid arthritis and osteitis deformans (Paget's disease). The author indicates that decalcification of the skeleton (osteoporosis) and a negative calcium balance occur in these conditions and that this is suggestive that a hyperparathyroid state may be partially responsible for the latter conditions although no definite evidence exists to establish this point. In addition to a solution of aluminum acetate, 1 pint of milk is given daily as a source of calcium and vitamin D. The author gives a prescription which contains "Liq. aluminum acetate (B. P.)" 1¼ ounces with a sufficient quantity of the vehicle (used to disguise the astringency of the drug) to make 4 ounces. The prescription calls for a minimum dose of 1 drachm four times daily after meals. The British Pharmacopeia describes no solution of aluminum acetate. It is therefore assumed that the author's prescription refers to the solution of aluminum acetate (Burow's solution) of the British Pharmaceutical Codex. On this basis it may be computed that the amount of aluminum acetate in the proposed prescription is approximately 7.2 per cent. The author states that the prescribed amount of aluminum acetate has a phosphate combining power to from 150 to 220 mg. of calcium. Under the author's discussion of rheumatoid arthritis, however, the average dose of aluminum acetate is stated to be 1 drachm of a 2.5 per cent solution four times a day. Apparently a weaker solution was employed for the cases of rheumatoid arthritis than for fibrocystic disease and osteitis deformans. The 15 cases of arthritis treated showed no significant change in the blood calcium and phosphorus or in the radiologic evidence, although clinical improvement occurred in all but 2. Some increase in bone density was observed in 2 of the 8 cases of Paget's disease treated and in all 4 of the cases of generalized fibrocystic disease.

Besides being too inadequate to establish definite conclusions, the evidence presented by the author appears questionable when it is realized that the daily intake of milk of most of the patients treated with aluminum acetate provides more phosphorus than can be expected to be removed by combination with the amount of the drug given. The author indicates that an attempt to find an adequate diet of a constant low phosphorus content was abandoned as impracticable. As has been indicated, unless the phosphorus income is deficient, the removal of phosphates by aluminum acetate is of no practical importance. Further studies appear to be necessary before the usefulness of aluminum acetate in secondary hyperparathyroid states and rheumatoid arthritis can be established.

BENIGN TUMORS OF GALLBLADDER

To the Editor:—What is the prognosis of a small adenoma at about the ampulla within the gallbladder in a woman aged 34? The gallbladder fills and empties promptly. There has been vague distress at intervals for two years, and the roentgenogram suggests periduodenal adhesions. The appendix does not fill. The gastrointestinal tract is otherwise normal. There is never any jaundice. No change in size has taken place since the roentgen examination six months ago. The patient is in excellent health, and conservative treatment with roentgen rays once a year is considered unless statistics show the tendency to malignancy is too great.

D. G. Dudley, M.D., Endicott, N. Y.

ANSWER.—Benign tumors of the gallbladder, although apparently rare, have been sufficiently studied in surgical and necropsy specimens to indicate that two general types probably occur: 1. Those secondary to chronic proliferative cholecystitis. These are usually multiple. 2. Polyps and adenomas (adenomyoma, myoma, lipoma, myxoma and fibroma), usually occurring singly and regarded by Kerr and Lendrum (*Brit. J. Surg.* **23**:615 [Jan.] 1936), in a review of the literature, as true tumors of the gallbladder in contradistinction to the first group.

The probability that such tumors may undergo malignant change seems to be small. Carcinoma of the gallbladder has been reported which appeared grossly like an adenoma (Lauritzen, S. H.: *Acta chir. Scandinav.* **79**:105, 1936. Eiserth, P.: Virchows Arch f. path. Anat. **302**:717, 1938). Presumably these tumors were not malignant from the onset. Eiserth found 13 adenomas, one of which showed microscopic evidence of malignancy, in approximately 4,000 gallbladders. These reports are chiefly concerned with stressing the possibility of malignant degeneration. On the basis of surgical and necropsy material it would appear that carcinoma may arise in papillomas or polyps of the gallbladder but that this has been observed in only a small proportion of the cases.

There is little, if any, evidence that polyps seen by cholecystography have undergone malignant change. Whether this indicates that polyps of gallbladders which concentrate dye sufficiently to visualize differ in their potentialities from clinically unrecognizable polyps is not known. It should be emphasized that an insufficient number of cases have been studied by cholecystography and eventually followed to operation or necropsy to justify statistical conclusions.

In view of these considerations and the fact that the diagnosis of polyp of the gallbladder by a competent roentgenologist has at times not been confirmed at operation or necropsy, medical management would seem to be the treatment of choice. Indications which would justify operation are (1) symptoms definitely referable to the biliary tract which fail to respond to medical treatment or (2) an increase in the size of the filling defect in the gallbladder (Walters, Waltman, and Snell, A. M.: Diseases of the Gall Bladder and Bile Ducts, Philadelphia, W. B. Saunders Company, 1940, p. 471).

ERUPTION OF TEETH

To the Editor:—A boy at the age of 4 fell and knocked out two teeth, the upper central and lateral incisors. A roentgenogram taken about a month later showed the permanent teeth well formed. This was four years ago, and these permanent teeth have not erupted. Several roentgenograms in the past year have shown the teeth well formed, and the dentist has been expecting them to grow out of the gum at any time for the past year. He is now a healthy, well developed boy of 8. He is about 2 inches taller than the average, and his weight is about average for his age. He was a bottle fed baby. He has had no serious illness except bronchopneumonia two years ago. His baby teeth were slow in developing. He has shed his remaining upper and lower incisors, and the permanent teeth have grown in normally. Any suggestions you can give to stimulate the growth of these teeth will be appreciated.

W. J. Graber, M.D., Beaumont, Texas.

ANSWER.—The eruption of the teeth appears to be related to periodontal vascularity. Vigorous rubbing, therefore, of the gingival tissue which overlies the unerupted teeth with the fingers and a tooth brush is likely to facilitate their eruption. If this procedure is not effective, it is possible that eruption has been delayed because of a mechanical obstruction of the overlying soft or even osseous structure, which normally should atrophy or become resorbed. The surgical removal of the overlying gum tissue or bone and the exposure of the incisal portions of the teeth are then indicated.

SENSITIVITY TO FACE POWDER AND PERFUME

To the Editor:—A patient is sensitive to orris root. She has a vasomotor rhinitis but will not use any hypoallergic powder. She buys expensive powder from the department stores, and they assure her that the powder is free from orris root, lead and rice. A cutaneous test with her new powder is positive but not so strong as with orris root. Are there any chemicals related to orris root in the ordinary powders which will sustain the symptoms? She is receiving injections. Will it be necessary for her to use only hypoallergic powder?

Elk Tannenbaum, M.D., New York.

ANSWER.—The only possible allergenic substance which may be included in powders and which may sustain the allergic symptoms, in the absence of orris root and rice starch, is wheat starch. Few cosmetic manufacturers use any starch in their powders, and orris root is rarely used. The probabilities are that the patient may be sensitive to the perfume used, since the vast majority of persons sensitive to face powders are also allergic to the essential oils. Of course in rare instances some people may be sensitive to the individual components of a cosmetic which would ordinarily be considered nonallergenic.

MUSHROOMS AND HYPERTENSION

To the Editor:—Can you advise me concerning the use of mushrooms in the treatment of high blood pressure? I know they long have been of some use, but I'd like to know what references there are on studies in the use of this succulent food. I know parsley and garlic are used as well.

John Fassett Edwards, M.D., Easton, Pa.

ANSWER.—There is no scientifically valid evidence that mushrooms have any therapeutic value in hypertensive arterial disease.

REDUCED SPERMATOZOAL FERTILITY

To the Editor:—May I take exception to the answer to the question headed "Few Motile Spermatozoa After Operation for Cryptorchism" in Queries and Minor Notes (April 12, 1941)? This stated that "at present there is no satisfactory method of inducing spermatogenesis." The man in question has a basal metabolic rate of minus 11, and a few motile spermatozoa were found in his specimen of spermatic fluid. The urologists of our sterility study group have been classifying in the relatively sterile, rather than absolutely sterile, group all men whose specimens show any spermatozoa at all, alive or dead. The reason for this is that some of these persons may be improved by proper treatment to fertility levels. The treatment consists of limited courses of stimulation by gentle prostatic massage, anterior pituitary-like sex hormone and obviously in this case thyroid substance, the latter over more prolonged periods. Vitamin E would seem also to be indicated. Our experience has been that the outlook for such a patient is by no means hopeless as far as spermatogenesis and children are concerned.

Paul Titus, M.D., Pittsburgh.